

Transport Phenomena in Biological Systems: A Textbook for Biomedical Engineers

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Understanding the physical, chemical and biological processes governing the movement of mass and transmission of forces throughout an organism is important in biomedical engineering and physiology. Transport processes influence the normal and pathological function of cells and organs. For the biomedical engineer, transport processes are important in the design and operation of a number of devices including those for kidney dialysis, removal of toxins, hybrid artificial organs, and drug delivery. Thus, this discipline is an important component of the undergraduate curriculum in biomedical engineering.

At Duke, we find that the traditional transport texts are not particularly helpful. Although these texts are often quite good for their intended audience in chemical or mechanical engineering, engineering concepts are not presented in the context of important biological problems. The absence of a sufficient presentation of biological concepts and problems limits the relevance of these texts and causes difficulties for students in applying the principles in all but the simplest problems. Based upon our experience, we have developed a set of course material consisting of chapters from selected texts, notes, and articles from the current literature. Although this assembly of material is an improvement upon the texts available, this approach is limited because students do not receive enough examples and the literature papers often do not present enough material for students to easily comprehend the application of transport models. Based upon these concerns we have decided to develop a textbook for a two semester undergraduate course sequence on transport phenomena in biological systems.

Our goals for the text on transport phenomena in biological systems are to present engineering fundamentals and biological applications in a unified way and to provide necessary skills to develop and critically analyze models of biological processes. The book will cover topics in fluid mechanics, mass transport and biochemical interactions (chemical reactions and binding interactions). The engineering concepts presented are motivated by specific biological problems. Applications of these concepts are discussed immediately after development of the engineering concepts. In this way the student will gain understanding of the specific topic presented as well as the application of the concept to important biological problems. Each chapter will contain a significant number of example and homework problems which elaborate upon problems discussed in the text or address new biomedical problems. Problems and examples will include analytical as well as numerical solutions. We will emphasize analytical solutions because these solutions can often provide important physical insights important for introductory material, even if the insight provides only a first order level of understanding. We will also cite current literature for those interested in more detailed analysis of problems of current interest.

We assume that the text will be used by students in their junior or senior year. We assume some exposure to biology but do provide some review material and reference relevant texts in cell biology and physiology. The students have not had any previous exposure to mass and momentum transport except for a brief discussion of diffusion in introductory chemistry. Although students will have been exposed to most of the mathematical concepts discussed in the text, we provide a review in the Appendix. We have found the review material very helpful in the course we have taught.

Text Outline The text contains an introduction and three parts. The Introduction provides the motivation for the text and its organization. The three parts examine concepts and biomedical applications in fluid mechanics, mass transport, and the effect of transport processes upon biochemical interactions. Each part begins with a chapter developing the relevant engineering concepts in terms of a specific biological context. In subsequent chapters, more detailed examples are considered so that students can understand the process of taking a biological problem and developing a model to address

quantitative questions. Although the text is designed for a two semester course, the text could be adapted for a single semester course by omitting some chapters which present detailed applications (e.g. chapters 4, 8-10, 15 and 16).

Biological problems examined include those at the molecular level (e.g. protein diffusion), cellular level (e.g. transport across endothelium), tissue level (e.g. transport in tumors or across the glomerulus), organ level (e.g. blood flow in organs) and organism level (e.g. pharmacokinetic models). Many of the problems are at the cellular and tissue level and fewer focus upon the organ and organism level. The reasons for this distribution are because understanding many problems at the cellular and tissue level simplifies development of organ level models. The problems themselves will involve analytical and numerical solutions of transport problems. Numerical solutions are provided with MATLAB although the problems will be general enough for solution by any number of packages. The outline is as follows.

Chapter 1. Introduction

- 1.1. Rationale and motivation
- 1.2. Definition of transport processes
- 1.3. Relative importance of convection and diffusion
- 1.4. Transport across and within cells
 - 1.4.1. Transport across the cell membrane
 - 1.4.2. Transport within the cell
- 1.5. Transcellular transport
 - 1.5.1. Epithelial cells
 - 1.5.2. Endothelial cells
- 1.6. Physiological transport systems
 - 1.6.1 The cardiovascular system
 - 1.6.2 Respiratory system
 - 1.6.3 Gastrointestinal system
 - 1.6.4 Liver
 - 1.6.5 Kidneys
 - 1.6.6 Integrated organ function
- 1.7. Application of Transport Processes in Disease Pathology, Treatment and Device Development
 - 1.7.1 Transport processes and atherosclerosis
 - 1.7.2 Transport processes and cancer treatment
 - 1.7.3 Transport processes and tissue engineering
- 1.8. Relative importance of transport and reaction processes
- 1.9. Overview of text
- 1.10. Questions
- 1.11. Problems
- 1.12. References

Part A. Fundamentals and Applications of Fluid Mechanics

- 2.1. Introduction
- 2.2. Kinematics
 - 2.2.1. Control Volumes
 - 2.2.2. Velocity Field
 - 2.2.3. Flow rate
 - 2.2.4. Acceleration
 - 2.2.5. Streamlines, Streamtubes and Streaklines
- 2.3. Conservation Relations
 - 2.3.1. Conservation of Mass
 - 2.3.2. Momentum Balances
 - 2.3.3. Forces
 - 2.3.4. Boundary Conditions
- 2.4. Fluid Statics
 - 2.4.1. Static Equilibrium
 - 2.4.2. Surface Tension
 - 2.4.3. Membrane and Cortical Tension

- 2.5. Constitutive Relations
 - 2.5.1. Newton's Law of Viscosity
 - 2.5.2. Non-Newtonian Rheology
 - 2.5.3. Time Dependent Viscoelastic Behavior
- 2.6. Laminar and Turbulent flow
- 2.7. Application of Momentum Balances
 - 2.7.1. Flow induced by a sliding plate
 - 2.7.2. Pressure-driven flow through a narrow rectangular channel
 - 2.7.3. Flow of a fluid through a cylindrical tube
 - 2.7.4. Flow of a power law fluid in a cylindrical tube
 - 2.7.5. Flow Between Rotating cylinders
- 2.8. Differential Form of the Conservation of Mass in Three Dimensions
- 2.9. Differential Form of the Conservation of Linear Momentum and Navier-Stokes Equation in Three Dimensions
- 2.10. Rheology and Flow of Blood
 - 2.10.1. Measurement of Blood Viscosity
 - 2.10.2. Rheology of Blood Flow in Large Tubes
 - 2.10.3. Fahreus-Lindquist effect
- 2.11. Questions
- 2.12. Problems
- 2.13. References

Chapter 3. Dimensional Analysis and Scaling

- 3.1. Dimensional analysis and dimensionless groups
- 3.2. Scaling and development of models to study flow in arteries
- 3.3. Low Reynolds number flow
- 3.4. Cell swimming
- 3.5. Flow in porous media
- 3.6. Fluid transport in the vitreous
- 3.7. Lubrication theory and flow of red cells in capillaries

Chapter 4. Fluid Flow in the Circulation and Tissues

- 4.1. Steady and unsteady flow in arteries
- 4.2. Flow in branched and curved vessels
- 4.3. Arterial fluid dynamics and atherosclerosis
- 4.4. Flow in the venous circulation
- 4.5. Flow in capillary networks
- 4.6. Flow in porous tissues

Chapter 5. Turbulent Flow and Macroscopic Balances for Momentum Transport

- 5.1. Turbulence
- 5.2. Turbulence in physiological fluid mechanics
- 5.3. Integral forms of the conservation of mass and linear momentum
- 5.4. Bernoulli's equation
- 5.5. Flow and pressure drop across heart valves

B. Fundamentals and Applications of Mass Transport

Chapter 6. Introduction to Mass Transport

- 6.1. Definitions and Fluxes
- 6.2. Diffusion as a Random Walk
- 6.3. Constitutive Relations
 - 6.3.1. Fick's Law of Diffusion for Dilute Solutions
 - 6.3.2. Multicomponent Diffusion; Stefan-Maxwell equation
- 6.4. Estimation of Diffusion Coefficients in Solution
 - 6.4.1. Stokes-Einstein Relation and Prediction of Diffusion Coefficients
 - 6.4.2. Correlations
- 6.5. Steady State Diffusion in One-Dimension
 - 6.5.1. Diffusion in Rectangular Coordinates

- 6.5.2. Diffusion in Cylindrical Coordinates
 - 6.5.3. Diffusion in Spherical Coordinates
 - 6.6. Unsteady Diffusion
 - 6.6.1. One-Dimensional Diffusion in a Semi-Infinite Medium
 - 6.6.2. One-Dimensional Unsteady Diffusion in a Finite Media
 - 6.6.3. Diffusion of a Solute into a Sphere from a Well-Stirred Bath
 - 6.7. Quasi-steady transport across membranes and determination of membrane permeability
 - 6.8. Diffusion-Limited Reactions
 - 6.8.1. Diffusion-Limited Binding and Dissociation in Solution
 - 6.8.2. Diffusion-Limited Binding between a Cell Surface Protein and a Solute
 - 6.8.3. Diffusion-limited Binding on a Cell Surface
- Chapter 7. Conservation of Mass for Dilute Solutions
- 7.1. Generalized conservation relations for binary systems
 - 7.2. Dimensional analysis
 - 7.3. Electrolyte transport and ion transport across membranes
 - 7.4. Diffusion and convection
 - 7.5. Interphase mass transport and mass transfer coefficients
 - 7.6. Boundary layer theory and correlations for mass transfer coefficients
- Chapter 8. Transport in Porous Media
- 8.1. Factors influencing solvent and solute transport in tissue
 - 8.2. Models of transport in porous media
- Chapter 9. Fluid and solute transport across endothelium and in tissues
- 9.1. Endothelial structure and summary of experimental observations
 - 9.2. Models of solute transport across capillaries
 - 9.3. Models of macromolecular transport in tissues
- Chapter 10. Solvent and solute transport across the kidney glomerulus
- 10.1. Anatomy and physiology of the kidney and glomerulus
 - 10.2. Role of osmotic pressure in solvent flow across the kidney
 - 10.3. Role of epithelial cells and basement membrane in transport across the glomerulus
- Chapter 11. Macroscopic Balances for Mass Transport
- 11.1. Integral forms of the conservation of mass and linear momentum
 - 11.2. Bernoulli's equation
 - 11.3. Flow and pressure drop across heart valves
 - 11.4. Integral forms of the conservation of mass for dilute solution
 - 11.5. Mass transport and design of an artificial kidney
- Part C. The Effect of Mass Transport upon Biochemical Interactions
- Chapter 12. Mass Transport and Biochemical Interactions
- 12.1. Chemical kinetics and reaction mechanisms
 - 12.2. Enzyme kinetics and antigen-antibody interactions
 - 12.3. Heterogeneous chemical reactions
 - 12.4. Combined mass transport and chemical reactions
 - 12.5. Effect of flow upon local concentrations in blood
 - 12.6. Lipoprotein transport and atherosclerosis
- Chapter 13. Oxygen transport from the lungs to tissues
- 13.1. Oxygen-hemoglobin binding kinetics and equilibrium
 - 13.2. Dynamics of oxygen transport and binding in the capillaries
 - 13.3. Oxygen delivery to tissues
 - 13.4. Heterogeneity of oxygen transport
- Chapter 14. Ligand-receptor kinetics on the cell surface and molecular transport within cells

- 14.1. Diffusion on cell membranes and through cells
- 14.2. Diffusion and binding on cell surfaces
- 14.3. Kinetic models of receptor-mediated endocytosis and receptor-ligand trafficking
- 14.4. Oxygen transport through cells and reaction in mitochondria

- Chapter 15. Cell adhesion and cell signaling
 - 15.1. Kinetic and thermodynamic models of cell adhesion
 - 15.2. Effect of diffusion on cell adhesion
 - 15.3. Cell signaling models
 - 15.4. Role of diffusion in G protein activation

- Chapter 16. Transport of drugs and macromolecules in tumors
 - 17.1. Tumor structure
 - 17.2. Transport properties
 - 17.3. Models of transport processes
 - 17.4. Effect of binding and drug metabolism upon drug uptake by tumors

- Chapter 17. Transport in Organs and Organisms
 - 18.1. Flow and transport based models
 - 18.2. Effect of heterogeneous capillary distribution upon transport in organs
 - 18.3. Scaling laws and relation to transport properties
 - 18.4. Physiologically based pharmacokinetic models
 - 18.5. Pharmacokinetic models and drug delivery

- Appendix. Relevant Mathematical Concepts
 - A.1. Review of calculus and solution of ordinary differential equations
 - A.2. Solution of partial differential equations
 - A.2.a. Characteristic value problems
 - A.2.b. Separation of variables
 - A.2.c. Laplace Transform methods
 - A.3. Basics of vectors and tensors
 - A.4. Numerical solution of ordinary and partial differential equations using MATLAB