MATHEMATICAL FOUNDATIONS AND BIOMECHANICS
OF THE DIGESTIVE SYSTEM

Mathematical modelling of physiological systems promises to advance our understanding of complex biological phenomena and pathophysiology of diseases. In this book, the authors adopt a mathematical approach to characterize and explain the functioning of the gastrointestinal system. Using the mathematical foundations of thin shell theory, the authors patiently and comprehensively guide the reader through the fundamental theoretical concepts, via step-by-step derivations and mathematical exercises, from basic theory to complex physiological models. Applications to nonlinear problems related to the biomechanics of abdominal viscera and the theoretical limitations are discussed. Special attention is given to questions of complex geometry of organs, effects of boundary conditions on pellet propulsion, as well as to clinical conditions, e.g. functional dyspepsia, intestinal dysrhythmias and the effect of drugs to treat motility disorders. With end-of-chapter problems, this book is ideal for bioengineers and applied mathematicians.

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To all those who gave so much, and were given so little
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Preface

Recent technological advances in various fields of applied science have radically transformed the strategies and vision of biomedical research. While only a few decades ago scientists were largely restricted to studying parts of biological systems in isolation, mathematical and computational modelling now enable the use of holistic approaches to analyse data spanning multiple biological levels and traditionally disconnected fields.

Mathematical modelling of organs and systems is a new frontier in the biosciences and promises to provide a comprehensive understanding of complex biological phenomena as more than the sum of their parts. Recognizing this opportunity, many academic centres worldwide have established new focuses on this rapidly expanding field that brings together scientists working in applied mathematics, mechanics, computer science, bioengineering, physics, biology and medicine. A common goal of this effort is to stimulate the study of challenging problems in medicine on the basis of abstraction, modelling and general physical principles.

This book is intended for bioengineers, applied mathematicians, biologists and doctors. It provides a brief and rigorous introduction to the mathematical foundations of thin-shell theory and its applications to nonlinear problems of the biomechanics of hollow abdominal viscera. It should be stressed that the text is not directed towards rigorous mathematical proofs of methods and solutions, but rather to a thorough comprehension, by means of mathematical exercises, of the essentials and the limitations of the theory and its role in the study of biomedical phenomena. The book can be used as a textbook for senior undergraduate and postgraduate students, although it may also be of interest to researchers and scientists who wish to obtain some general background knowledge of shell theory.

The approach is facilitated by the introduction of basic concepts of the theory of surfaces (Chapter 1), which are essential prerequisites for a subsequent understanding of the theory of shells. The mathematical techniques employed are reasonably elementary, and require knowledge of calculus and vector algebra. Throughout the
text we deliberately use non-tensorial notation, since tensor calculus is not included in the normal curriculum for bioengineering and applied-mathematics students.

There are only a few places in the book where the use of tensors was necessary.

In Chapter 2 the method of fictitious tangent deformation is introduced. Questions of parameterization of shells of complex geometry, which are common in practical applications, e.g. modelling of abdominal viscera, are considered.

The general theory and the governing system of equations for thin shells, without any restrictions on the magnitude of the displacements, rotations, or strains, are formulated in Chapter 3. The dimensional reduction is achieved by formal integration of the equations of equilibrium of a three-dimensional solid over the thickness of the shell and a successful application of the second Kirchhoff–Love hypothesis. The equations of equilibrium of the shell are derived in general curvilinear and orthogonal coordinates.

Part of the aim of the book is to gain insight into the biomechanics of soft biological tissues, namely the wall of the abdominal viscera, in particular by analysing their structure, morphology and electrical phenomena at multihierarchical levels of organization. Thus, in Chapter 4 the main consideration is given to a phenomenological continuum mechanics approach to derive constitutive relations for the biocomposite. It is treated as a three-phase mechanochemically active medium.

Chapter 5 is dedicated to boundary conditions. Organs of the digestive tract have a strong ligamentous support as well as multiple sphincters that are located at the site of organ junctions. Such arrangements, e.g. gastro-oesophageal, gastroduodenal and ileocaecal junctions, severely restrict the deformability of the organ in that region. Therefore, only small deformations on the boundary are considered.

Chapter 6 is devoted to the theory of soft shells, where fundamental hypotheses and general criteria for the co-existence of various stress–strained states are formulated and the governing system of equations is derived. The dynamic approach, which is oriented towards numerical solutions, is developed throughout.

The material about the nonlinear theory of thin shells presented in the book is well known. The reader is advised to consult texts by Galimov (1975), Ridel and Gulin (1990), Galimov et al. (1996), Ventsel and Krauthammer (2001), Taber (2004), and Libai and Simmonds (2005) for full information. The original contribution and the strength of this book, though, are in applications of the theory to model and to study the biomechanics of the gastrointestinal system, in particular the stomach, small intestine and colon. Attention is paid to the biological plausibility of the basic modelling assumptions which are crucial in selection of appropriate mathematical models. Electrical, chemo-electrical and mechanical phenomena have been integrated at various levels of models to simulate and analyse coupled processes, e.g. electromechanical waves of deformation and the propulsion of a solid bolus, that comprise the fundamental physiological principles of functionality of the gastrointestinal system.
Preface

Special attention is paid to simulations of clinically meaningful problems, namely the motility of the stomach and of the small and large intestines in normal and pathological conditions, e.g. functional dyspepsia, gastroparesis and intestinal dysrhythmia, and to the analysis of underlying physiological mechanisms from biomechanical perspectives. In Chapter 7 the problem of electromechanical wave activity in the stomach is analysed. The effects of localized and spatially distributed pacemakers, intraluminal pressure, mechanical characteristics of the tissue and pharmacologically active compounds on the dynamics of the stress–strain distribution in the organ are investigated.

Chapter 8 is dedicated to the dynamics of a cylindrical soft shell – a model of a functional unit of the small intestine. Patterns of myoelectrical activity in normal and pathological conditions are reproduced numerically. Particular attention is paid to the self-sustaining electromechanical wave phenomenon that mimics intestinal dysrhythmia and its pharmacological attenuation.

The biomechanics of propulsion of a solid bolus along the colon is studied in Chapter 9. The effects of various types of boundary conditions at the aboral end are investigated. The emphasis is placed on an analysis of the effects of promotility drugs on the dynamics of propulsion.

Biological and clinical applications of mathematical modelling are discussed in Chapter 10. Attention is paid to future developments and improvements of existing mathematical models of the abdominal viscera. Electrophysiological and neuropharmacological aspects of gastrointestinal motility, together with the key role of intrinsic neuronal pathways, multiple neurotransmission and extrinsic regulatory nervous control elements are emphasized.

Each of the chapters is followed by a set of problems, which can be used by the reader to check his or her understanding of the subject matter. Some problems bring out additional details that are not considered in the main body of the text.

This book was written in many places: Kazan State University (Tatarstan, Russia), the Arabian Gulf University (Kingdom of Bahrain), the National Core Research Centre for Systems Bio-Dynamics and Pohang University of Science and Technology (South Korea). We would like to thank our colleagues who have contributed both directly and indirectly to this book. We are particularly grateful to Dr W. Morrison for reviewing the manuscript and providing corrections and valuable comments. Finally, we wish to extend our thanks to the publisher, Cambridge University Press, and especially to Dr M. Carey, Publishing Editor, and Ms C. L. Poole, Assistant Editor, who supported the project from the very beginning and made its successful publication possible.

Professor Dr R. Miftahof
Professor H. G. Nam
Notation

\[ S_0, S, \dot{S} \]
cut, undeformed, and deformed (*) middle surface of a shell, respectively

\[ S_z \]
surface co-planar to \( S \) such that \( S_z \parallel S \)

\[ S^r \]
middle surface of a net

\[ \Sigma, \dot{\Sigma} \]
boundary faces of an undeformed shell and a deformed shell, respectively

\[ d\Sigma, d\dot{\Sigma} \]
differential line elements on \( \Sigma \) and \( \dot{\Sigma} \), respectively

\[ h \]
thickness of a shell

\[ x_1, x_2, x_3 \]
rectangular coordinates

\[ r, \varphi, z \]
cylindrical coordinates

\[ \{i_1, i_2, i_3\} \]
ortogonal base of \( \{x_1, x_2, x_3\} \)

\[ \{k_1, k_2, k_3\} \]
ortogonal base of \( \{r, \varphi, z\} \)

\[ (a_1, a_2), (\dot{a}_1, \dot{a}_2) \]
curvilinlear coordinates of the undeformed and deformed shell, respectively

\[ \bar{m}, \dot{m} \]
vectors normal to \( S \) and \( \dot{S} \), respectively

\[ \bar{r}, \bar{r}^2, \bar{r}^3 \]
tangent vectors to lines on \( S, \dot{S}, \dot{\Sigma} \) or their boundaries, respectively

\[ \bar{n}, \bar{n}^r, \bar{n}^z \]
normal vectors to lines on the boundaries of \( S, \dot{S} \) and \( \dot{\Sigma} \), respectively

\[ \bar{r}, \bar{\rho}, \bar{\rho} \]
position vectors of points \( M \in S, \dot{M}_z \in S_z \) and \( \dot{M}_z \in \dot{S}_z \), respectively

\[ \bar{r}_i, \bar{\rho}_i \]
tangential vectors to coordinate lines on \( S, S_z \), respectively

\[ \{\bar{r}_1, \bar{r}_2, \bar{m}\}, \{\bar{r}_1^2, \bar{r}_3^2, \bar{m}\} \]
covariant and contravariant bases at a point \( M \in S \), respectively

\[ \{\bar{\rho}_1, \bar{\rho}_2, \bar{\rho}_3\} \]
covariant base at point \( \dot{M}_z \in S_z \)
orthogonal bases on $\Sigma$ and $\tilde{\Sigma}$, respectively
angles between coordinate lines defined on $S$, $S_z$, and $\tilde{S}$, respectively
shear angle
Lamé coefficients on $S$, $S_z$, and $\tilde{S}$, respectively
components of the metric tensor
determinants of the metric tensor
components of the second fundamental form
unit base vectors on $S$, $S_z$, and $\tilde{S}$, respectively
lengths of line elements on $S$, $S_z$, and $\tilde{S}$, respectively
surface area of a differential element of $S$
Christoffel symbols of the first and second kind, respectively
deviator of the Christoffel symbols
projection of the displacement vector on $x_1$, $x_2$, and $x_3$ axes, respectively
components of the tensor of planar deformation through points $M \in S$ and $M_z \in S_z$, respectively
physical components of the tensor deformation in undeformed and deformed configurations of a shell, respectively
principal physical components of the tensor of deformation, respectively
elastic and viscous parts of deformation, respectively
components of deformation of the boundary of a shell in $\tilde{n}$, $\tilde{r}$ directions
components of the tensor of tangent and bending fictitious deformations, respectively
stretch ratios (subscripts $c$ and $l$ refer to the circular and longitudinal directions of a bioshell)
principal stretch ratios
invariants of the tensor of deformation
components of bending deformation and twist of the boundary of a shell in $\tilde{n}$, $\tilde{r}$ directions
rotation parameters
rotation parameters in fictitious deformation
normal curvatures of $S$ and $\tilde{S}$, respectively
Notation

\( k_{ik}, \dot{k}_{ik} \) twist of \( S \) and \( \dot{S} \), respectively
\( k_n, k_\tau, k_n^*, k_\tau^* \) normal curvatures in \( \hat{n}, \hat{\tau}, \hat{n}^* \) and \( \hat{\tau}^* \) directions, respectively
\( k_{nt}, k_{n\tau} \) twist of the contours \( \Sigma \) and \( \dot{\Sigma} \), respectively
\( 1/R_{1,2}, 1/R_{1,2}^\tau \) principal curvatures of \( S \) and \( \dot{S} \), respectively
\( K, K_0 \) Gaussian curvatures of \( S \) and \( \dot{S} \), respectively
\( \Delta K \) increment of the Gaussian curvature
\( e_{a_1}, e_{a_2} \) elongations in directions \( a_1 \) and \( a_2 \), respectively
\( L_i^1(T_{ik}), L_i(T_{ik}) \) differential operators
\( d\Sigma_2, d\Sigma_2^\tau \) surface area of a differential element of \( \dot{\Sigma} \)
\( d\sigma, d\Omega \) free surface area of a shell
\( d\Omega \) unit volume of an element of a shell
\( p \) pressure
\( \vec{p}_i \) stress vectors
\( F_c \) contact force
\( F_d \) force of dry friction
\( \vec{R} \) resultant of force vectors
\( \vec{M}_i \) resultant moment vector of internal forces
\( \vec{p}_{(+)}, \vec{p}_{(-)} \) external forces applied over the free surface area of a shell
\( \vec{p}_n^* \) normal stress vector on \( \dot{\Sigma} \)
\( \vec{F} \) vector of mass forces per unit volume of the deformed element of a shell
\( \vec{X} \) resultant external force vector on \( \dot{S} \)
\( \vec{M} \) resultant external moment of external forces on \( \dot{S} \)
\( \vec{T}_{ii}, \vec{T}_{ik} \) normal, shear and lateral forces per unit length of a shell parallel to \( \dot{S} \), respectively
\( T_{e_1}, T_{e_2}, T_m \) total force per unit length
\( T^p_{e_1}, T^a_{e_1}, T^a_{e_2} \) passive and active components of the total forces per unit length, respectively
\( T^1, T^2 \) forces per unit length of reinforced fibres
\( T_{11}, T_{22} \) principal stresses
\( I^1, I^2(T) \) invariants of the stress tensor
\( \dot{M}_{ii}, \dot{M}_{ik} \) bending and twisting moments per unit length of a shell perpendicular to directions \( a_1 \) and \( a_2 \) on \( \dot{S} \)
\( \vec{M}_i \) projections of the moment vector on \( \dot{e}_1, \dot{e}_2, \dot{m} \)
\( \vec{X}_i \) projections of the external force vector on \( \dot{e}_1, \dot{e}_2, \dot{m} \)
\( \vec{R}_n \) resultant force vector per unit length acting on \( d\Sigma_2 \) in the \( \dot{n} \) direction
Notation

- $\overline{M}_n$: resultant moment vector per unit length acting on $d\Sigma_2$ in the $\hat{n}$ direction
- $\hat{G}_z, \hat{H}$: bending and twisting moments in a boundary of a shell
- $\overline{G}_r, \overline{M}_p, \overline{M}_q$: resultant moment vectors per unit length of a soft shell
- $\sigma_{ij}$: stresses in a shell
- $\sigma^n_{ij}$: stresses in phase $\alpha$ of a biomaterial
- $c_{11}, \ldots, c_{14}$: material constants
- $d_m$: diameter of smooth muscle fibre
- $L$: length of bioshell/muscle fibre
- $\bar{S}_{c1}$: cross-sectional area of smooth muscle syncytia (SM)
- $v_{x_1}, v_{x_2}, v_{x_3}$: components of the velocity vector
- $k_v$: viscosity
- $\eta_{sp}$: coefficient of viscous friction
- $\rho, \rho^*$: densities of undeformed and deformed material of a shell, respectively
- $\rho^\alpha_\zeta$: partial density of the $\zeta$th substrate in phase $\alpha$ of a biomaterial
- $m^\alpha_\zeta$: mass of the $\zeta$th substrate in phase $\alpha$ of a biomaterial
- $\bar{u}_i, \bar{u}^\alpha$: total and elementary volumes of a biomaterial, respectively
- $c^\alpha_\zeta$: mass concentration of the $\zeta$th substrate in phase $\alpha$ of a biomaterial
- $\eta$: porosity
- $Q^\alpha_c, Q^\alpha_\zeta, Q_\zeta$: influxes of the $\zeta$th substrate into phase $\alpha$, external sources and exchange flux between phases, respectively
- $v^\zeta_{cj}$: stoichiometric coefficient in the $j$th chemical reaction
- $U^{(\alpha)}$: free energy of phase $\alpha$
- $S^{(\alpha)}_c, S^{(\alpha)}_\zeta$: entropy of phase $\alpha$ and partial entropy of the entire biomaterial, respectively
- $T$: temperature
- $\mu^\alpha_\zeta$: chemical potential of the $\zeta$th substrate in phase $\alpha$ of a biomaterial
- $\overline{q}$: heat-flux vector
- $R$: dissipative function
- $\Lambda_j$: affinity constant of the $j$th chemical reaction
- $I_{i1}, I_{i2}$: intracellular (i) and extracellular (o) ion currents
- $I_{m1}, I_{m2}$: transmembrane ion currents (SM)
- $I_{\text{ext}(i)}$: external membrane current (ICC)
- $I_{\text{ion}}$: total ion current (SM)
\[ I_{Ca}^-, I_{Na}, I_{K} \]

\[ \psi_i, \psi_o \]

\[ V_m, V_i, V_{c_{11}}, V_{c_{12}} \]

\[ V_{Ca}, V_{K}, V_{Cl} \]

\[ C_m, C_s \]

\[ R_{ms}, R_{ICC} \]

\[ g_{ij}, g_{0ij}, g_{i}^{\text{max}}, g_{o}^{\text{max}} \]

\[ m, h, n, x_{Ca} \]

\[ \alpha_y, \beta_y \]

\[ \lambda, \rho, \tau_x \]

\[ [Ca^{2+}] \]

\[ [Na^{+}]_i \]

\[ \delta_{Ca} \]

\[ \lambda, \psi_{Ca}, \tau_{Ca} \]

\[ \text{Ca}^{2+}, \text{Ca}^{2+}-\text{activated} \ K^+, K^+ \text{and} \ Cl^- \text{ion currents in} \]

\[ \text{smooth muscle, respectively} \]

\[ \text{Ca}^{2+}, \text{Ca}^{2+}-\text{activated} \ K^+, Na^+, K^+ \text{and} \ Cl^- \text{ion currents, respectively} \]

\[ \text{electrical potentials} \]

\[ \text{transmembrane potential} \]

\[ \text{membrane potential of the interstitial cell of Cajal} \]

\[ \text{membrane potentials in circular and longitudinal smooth} \]

\[ \text{muscle (SM), respectively} \]

\[ \text{reversal potentials for} \ Ca^{2+}, \ K^+ \text{and} \ Cl^- \text{currents in} \]

\[ \text{smooth muscle, respectively} \]

\[ \text{reversal membrane potentials for} \ Ca^{2+}, Ca^{2+}-\text{activated} \]

\[ \text{K}^+, Na^+, K^+ \text{and} \ Cl^- \text{ion currents for interstitial cells of} \]

\[ \text{Cajal, respectively} \]

\[ \text{membrane capacitance (SM)} \]

\[ \text{membrane capacitance (ICC)} \]

\[ \text{membrane resistance (SM)} \]

\[ \text{input cellular resistance (ICC)} \]

\[ \text{specific membrane resistance of a muscle fibre} \]

\[ \text{maximal intracellular (i) and extracellular (o) conductivities} \]

\[ \text{maximal conductances for ion currents of respective} \]

\[ \text{ion channels (SM)} \]

\[ \text{maximal conductances of voltage-dependent} Ca^{2+} \]

\[ \text{(N-type),} Ca^{2+}-\text{activated} \ K^+, Na^+, K^+ \text{and} Cl^- \text{channels} \]

\[ \text{(ICC), respectively} \]

\[ \text{dynamic variables of ion currents (SM)} \]

\[ \text{dynamic variables of respective ion currents (ICC)} \]

\[ \text{activation and deactivation parameters of ion channels} \]

\[ \text{(SM), respectively} \]

\[ \text{activation and deactivation parameters of ion channels} \]

\[ \text{(ICC), respectively} \]

\[ \text{‘biofactor’} \]

\[ \text{intracellular concentration of} Ca^{2+} \text{ions (SM)} \]

\[ \text{intracellular concentration of free} Ca^{2+} \text{ions (ICC)} \]

\[ \text{parameter of calcium inhibition (ICC)} \]

\[ \text{electrical numerical parameters and constants} \]
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<tr>
<td>$R_{sp}$</td>
<td>radius of a solid sphere</td>
</tr>
<tr>
<td>$Z_c$</td>
<td>position of the centre of a sphere</td>
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<tr>
<td>$\hat{V}, \dot{V}$</td>
<td>initial and current intraluminal volume, respectively</td>
</tr>
<tr>
<td>$W$</td>
<td>strain energy density function</td>
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<td>SM</td>
<td>smooth muscle syncytium</td>
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<tr>
<td>ICC</td>
<td>interstitial cells of Cajal</td>
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