Preface

"Long ago it became evident that the key to every biological problem must finally be sought in the cell, for every living organism is, or at some time has been, a cell."(The Cell in Development and Heredity, Macmillan, Inc., 1925, by Edmund B. Wilson).

However, the cell itself and various cell-associated objects (CAO) are products of evolution and are still in a state of development as any other so-called evolutionary systems (ES).

So, it is natural to use mathematical models (MM) or mathematics of development to better understand the cell and CAO.

This volume is devoted to mathematical modeling of the cell and cell processes based on novel MM of development. These MM are Volterra-like non-linear dynamic models that allow us to model problems of analysis and synthesis for a wide class of ES, in particular, the cell and CAO. CAO relate to separate parts of the cell and various systems of cells including tissues, organs, subsystems of an organism, and whole organisms.

The main features of these MM may offer descriptions of the cell and CAO creation and restoration processes, of dynamics of elimination or reservation of obsolete "technology" in them, of dynamics of resources distribution for fulfillment of internal and external functions of the cell and CAO, etc.

There are potentially unlimited uses of these MM due to the unlimited quantity of different biological systems that can be integrated at various levels of their consideration, including at the molecular or Human Genome levels.

At the same time, the monograph contains a survey of well known MM of life sciences (Part I of the book), and also a comparison of wide-accepted and novel models (in various parts of the book). Of course, this novel approach does not belittle other approaches, but rather complements and hopefully enriches them.

One of the reviewers believes that this book is essential because the subject has great potential and is not well covered in the literature.

The audience of this book includes researchers in life sciences and students of applied mathematics, especially those with an interest in mathematical applications to cell biology, immunology, medicine, and health care.

The book consists of both the general theory of modeling and various applications.

The base MM of development and their various complications as well as examples of applications of these MM to many problems of the cell and CAO can be found in Part II of the book.

One of the main complications for successful modeling of the cell and CAO consists of proper description of objects and of proper identification of the respective MM. Therefore, special parts of the book are devoted first to biological background of the objects and then to the problems and the methods of identification of initial data of the models.

In particular, the book contains descriptions of the main known facts of cell biology and immunology with the point of view of a mathematician who wants to carry over those facts onto the language of MM.

In the cell and CAO, genes of the entire genome often give necessary characteristics for MM. Therefore, serious attention is devoted to the exploration of various genes and proteins.

The authors feel that the results obtained from statements above confirm the importance and the reliability of the novel technique as well as add to the rapid growth of possibilities for mathematical modeling of progressively more complicated cell processes as time passes and as new information is gathered.

Recently, in particular, many important biological experimental results are related to the problems of regulation of cell processes (i.e., their dynamics). Some of them have been described and investigated here with the help of MM under consideration.

The general mathematical theory represented in the Appendix is mainly devoted to the existence and the uniqueness of solutions for the systems of relations of MM and for respective optimization problems. Considerable attention is also devoted to asymptotic properties of the solutions and to the qualitative investigation of the solution structure for the optimization problems.

In addition, a specific part of the Appendix is focused on respective optimal numerical methods and software. The solution of Volterra-type integral equations with pre-assigned accuracy by the optimal methods is stated and investigated. Reduction of many other problems to the solution of Volterra-type equations is analyzed.

Introduction to applications is devoted mainly to AIDS, cancers, and life longevity problems (Part III of the book).

The monograph is a further development of the techniques for modeling of ES, represented for the first time in the book *Model Development and Optimization*, KAP, 1999, by V. V. Ivanov.

Essential differences consist of detailed investigation of such complicated objects as the cell and CAO, and more complete results of the general mathematical theory of ES modeling are presented.

The main purpose of any investigation in life sciences is finding new effective ways for disease-targeted research and for cure of life-threatening diseases. We attempt to reach this purpose.

However, the experience of application of MM in trying to reach this goal shows that progress here depends on power of connection among specialists in various fields.

As a rule, mathematicians attempt to understand the results of biologists, but not the other way around. Many biologists believe that so far only methods of mathematical statistics may be useful to them.

In this regard, we would like to emphasize special capability of mathematicians to separate essential factors from unessential due to mathematicians' long training in abstract thinking. It means that mathematicians can be very useful for different complicated problems (including biological), and, of course, for formalization of these problems by means of MM. After this, experienced mathematicians can analyze those MM and provide useful feedback to biologists.

One of the special concerns of any scientific endeavor is the effort to acquire accurate measurement in a form that can be understood and verified by others. We would like to emphasize the New International System of Units (S.I.) that recognizes seven basic units: mass (Kilogram - kg), length (Meter - m), time (Second - s or sec), electric current (Ampere - A), temperature (Kelvin - K), luminous intensity (Candela – cd), and quantity of a substance (Mole – mole). The recommended use is the joule (J) rather than the calorie (cal) as the standard unit of energy (one J = 1 kgm^2/s^2 = 0.239 cal). In physics, energy is expressed usually in electron volts, ergs, or inverse centimeters. The relations between these units are 1 eV = 1.602 10^{-12} erg = 8066.1sm^{-1} = 23.05 kcal/mole.

Finally, the authors would like to express thanks to reviewers for fruitful criticism, to Dr. Keith Jones, Publisher of Elsevier, and to Andy Deelen, Administrative Editor Physics, Mathematics, Computer Science and Astronomy Department, for their help and concern about the fate of this book.

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