МИНИСТЕРСТВО ОБРАЗОВАНИЯ И НАУКИ
РОССИЙСКОЙ ФЕДЕРАЦИИ
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Математическое моделирование биологических процессов

Учебно-методическое пособие

Рекомендовано методической комиссией факультета ФИС
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В настоящем пособии изложены учебно-методические материалы по курсу “Математическое моделирование биологических процессов” для иностранных студентов, обучающихся в ННГУ по направлению подготовки 38.04.02. «Биология» (магистратура).

Учебно-методическое пособие предназначено для студентов факультета иностранных студентов обучающихся по направлению подготовки 38.04.02. «Биология» и может быть использовано как для работы в аудитории, так и для самостоятельной работы.

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MATHEMATICAL MODELLING OF BIOLOGICAL PROCESSES

Tutorial

Recommended by the Methodical Commission
of the Faculty of International Students for International Students,
studying at the M.Sc. Programme 38.04.02. "Biology" in English

Nizhni Novgorod

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Contents

Preface

This book refer to a university course delivered at the Lobachevsky University to students attending the Lectures on Mathematical Modelling in the frames of of the Master of Sciences Programmes.

The Lectures Notes devoted to modelling issues to show how the application of models to describe real world phenomena generates mathematical problems to be solved by appropriate mathematical methods.

The models dealt with in these Lecture Notes are quite simple, proposed with tutorial aims, while relatively more sophisticated models arising in the real scientific researches. In the process of preparation of the given manual a plenty of remarkable university textbooks and special monographies has been used. In some cases, not hoping to surpass authors of these magnificent books in clearness and presentation of a statement, we used entirely the most successful (from our point of view) fragments of those or other sources with the indication on their authorship. In some cases we made insignificant updatings of the text (not changing its sense) for the best coordination of various parts of the manual.

The contents containes four chapters. The first and second Chapters proposes an introduction to the method of mathematical modelling – An Intuitive Introduction to Modelling and Some technological details of the Mathematical Modelling (see [Bellomo N., De Angelis E., Delitala M., 2007], [Bellomo N., 2007], [Witelski T., Bowen M., 2015] et al). The third Chapter proposes some material connected with Continuous Population Models for Single Species, the the fourth chapter – with Discrete Population Models for Single Species. Mathematical models of dynamics of two interacting biological populations is dedicated to the fifth chapter. Finally, the sixth chapter is devoted to Some Mathematical models of Neuroscience.

In the course of drawing up the manual the author used a set of sources. All of them are brought in the list of references. Not always in the text exhaustive references to these sources are given: too frequent references to this or that source split up a statement of material and complicate his perception.The Lecture Notes look at application focussing on modelling and computational issues, while the pertinent literature on analytic methods is brought to the attention of the interested reader for additional education.

After the above introduction to the contents and aims of the Lecture Notes, a few remarks are stated to make a little more precise a few issues that have guided their redaction.

- All real systems can be observed and represented at different scales by mathematical equations. The selection of a scale with respect to others belong, on one side, to the strategy of the scientists in charge of deriving mathematical models, and on the other hand to the specific application of the model.
- Systems of the real world are generally nonlinear. Linearity has to be regarded either as a very special case, or as an approximation of physical reality. Then methods of nonlinear analysis need to be developed to deal with the application

of models. Computational methods are necessary to solve mathematical problems generated by the application of models to the analysis and interpretation of systems of real world.

- Computational methods can be developed only after a deep analysis of the qualitative properties of a model and of the related mathematical problems. Different methods may correspond to different models.
- Modelling is a science which needs creative ability linked to a deep knowledge of the whole variety of methods offered by applied mathematics. Indeed, the design of a model has to be precisely related to the methods to be used to deal with the mathematical problems generated by the application of the model.

These Lectures Notes attempt to provide an introduction to the above issues. We hope, that the given Lectures Notes will help students to achieve deeper understanding of the method of mathematical modelling and its opportunities.

Unit 1. An Intuitive Introduction to Modelling

> "Everything should be made as simple as possible, but not simpler".
>
> *Albert Einstein* [1]

> "… not to produce the most comprehensive descriptive model, but to produce the simplest possible model that incorporates the major features of the phenomenon of interest".
>
> *Howard Emmons*[2]

1.1. Some basic notions and definitions

The analysis of systems of applied sciences, e.g. technology, economy, biology etc, needs a constantly growing use of methods of mathematics and computer sciences. In fact, once a physical system has been observed and phenomenologically analyzed, it is often useful to use mathematical models suitable to describe its evolution in time and space. Indeed, the interpretation of systems and phenomena, which occasionally show complex features, is generally developed on the basis of methods which organize their interpretation toward simulation. When simulations related to the behavior of the real system are available and reliable, it may be possible, in most cases, to reduce time devoted to observation and experiments.

Bearing in mind the above reasoning, one can state that there exists a strong link between applied sciences and mathematics represented by mathematical models designed and applied, with the aid of computer sciences and devices, to the simulation of systems of real world. The term "mathematical sciences" refers to various aspects of mathematics, specifically analytic and computational methods, which both cooperate to the design of models and to the development of simulations.

Before going on with specific technical aspects, let us pose some preliminary questions:

- What is the aim of *mathematical modelling*, and what is a mathematical model?
- There exists a link between *models* and *mathematical structures*?
- There exists a correlation between *models* and *mathematical methods*?
- Which is the relation between *models* and *computer sciences*?

Moreover:

- Can mathematical *models* contribute to a deeper understanding of the *real systems*?
- Is it possible to reason about a *science of mathematical modelling*?

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[1] See [Einstein A., 1934], [Einstein A., 2015].
[2] See, for example, [Banerjee S., 2014; P.1].

- Can *education in mathematics* take some advantage of the above mentioned science of mathematical modelling ?

Additional questions may be posed. However, it is reasonable to stop here considering that one needs specific tools and methods to answer precisely to the above questions.

Nevertheless an intuitive reasoning can be developed and some preliminary answers can be given:

- Mathematical models are designed to describe physical systems by equations or, more in general, by logical and computational structures.
- The above issue indicates that *mathematical modelling* operates as a science by means of methods and mathematical structures with well defined objectives.
- Intuitively, it can be stated that education in mathematics may take advantage of the science of mathematical modelling. Indeed, linking mathematical structures and methods to the interpretation and simulation of real physical systems is already a strong motivation related to an inner feature of mathematics, otherwise too much abstract. Still, one has to understand if modelling provides a method for reasoning about mathematics.

At this stage of consideration the following definition of *mathematical model* can be introduced. This concept needs the preliminary definition of two elements:

- *Independent variables*, generally time and space;
- *State variables* which are the *dependent variables*, that take values corresponding to the independent variables;

Then the following concept can be introduced:

- *Mathematical model*, that is a set of equations which define the evolution of the state variable over the dependent variables.

The general idea is to observe the phenomenology of a real system in order to extract its main features and to provide a model suitable to describe the evolution in time and space of its relevant aspects. Bearing this in mind, the following definitions may be proposed:

Independent variables

The evolution of the real system is referred to the ***independent variables*** *which, unless differently specified, are time t, defined in an interval* ($t \in [t_0, T]$)*, which refers the observation period; and space* x*, related to the volume* V*,* ($x \in V$) *which contains the system.*

State variable

The ***state variable*** *is the finite dimensional vector variable*

$$u = u(t, x), \quad u(\cdot,\cdot):[t_0, T] \times V \rightarrow \mathbf{R}^n$$

where $u = col\{u_1, u_2, ..., u_n\}$ *is deemed as sufficient to describe the evolution of the physical state of the real system in terms of the independent variables.*

Mathematical model

A ***mathematical model*** *of a real system is an evolution equation suitable to define the evolution of the state variable u in charge to describe the physical state of the system itself.*

In order to handle properly a mathematical model, the number of equations and the dimension of the state variable must be the same. In this case the model is defined consistent:

Consistency

The mathematical model is said to be consistent if the number of unknown dependent variables is equal to the number of independent equations.

This means that one has to verify whether an equation belonging to the model can be obtained combining the remaining ones. If this is the case, that equation must be eliminated.

The real physical system may be interacting with the outer environment or may be isolated. In the first case the interactions has to be modelled.

Closed and Open Systems

A system is closed if it does not interact with the outer environment, while it is open if it does.

The above definitions can be applied to real systems in all fields of applied sciences: engineering, natural sciences, economy, and so on. Actually, almost all systems have a continuous distribution in space. Therefore, their discretization, that amounts to the fact that u is a finite dimensional vector, can be regarded as an *approximation* of real system.

In principle, one can always hope to develop a model which can reproduce exactly physical reality. On the other hand, this idealistic program cannot be practically realized considering that real systems are characterized by an enormous number of physical variables.

So, every mathematical model contains some uncertainties connected with variables and processes, which were omitted in the process of construction of model

The statement of mathematical problems need some data (e.g. the initial position of the system). Their measurements are affected by errors so that their knowledge may be uncertain.

In some cases this aspect can be dealt with by using in the model and/or in the mathematical problems randomness modelled by suitable stochastic variables. The solution of the problem will also be represented by random variables, and methods of probability theory will have to be used.

As rule mathematical models are stated in terms of evolution equations (for example – the system of ordinary differential equations). The above equations cannot be solved without complementing them with suitable information on the behavior of the system corresponding to some values of the independent variables. In other words the solution refers to the mathematical problem obtained linking the model to the above mentioned conditions. Once a problem is stated suitable mathematical methods have to be developed to obtain solutions and simulations, which are the prediction provided by the model.

1.2. Modelling Scales and Representation

As we have seen by the definitions proposed in Section 1.1, the design of a mathematical model consists in deriving an evolution equation for the dependent variable, which may be called state variable, which describes the physical state of the real system, that is the object of the modeling process.

The selection of the state variable and the derivation of the evolution equation begins from the phenomenological and experimental observation of the real systems. This means that the first stage of the whole modeling method is the selection of the observation scale. For instance one may look at the system by distinguishing all its microscopic components, or averaging locally the dynamics of all microscopic components, or even looking at the system as a whole by averaging their dynamics in the whole space occupied by the system.

For instance, if the system is a gas of particles inside a container, one may either model the dynamics of each single particle, or consider some macroscopic quantities, such as mass density, momentum and energy, obtained averaging locally (in a small volume to be properly defined: possibly an infinitesimal volume) the behavior of the particles. Moreover, one may average the physical variables related to the microscopic state of the particles and/or the local macroscopic variables over the whole domain of the container thus obtaining gross quantities which represent the system as a whole. The above approaches sometimes called, respectively, *microscopic modelling* and *macroscopic modelling*.

As an alternative, one may consider the microscopic state of each microscopic component and then model the evolution of the statistical distribution over each microscopic description. Then one deals with the *kinetic type* (*mesoscopic*) modeling. Modelling by methods of the mathematical kinetic theory requires a detailed analysis of microscopic models for the dynamics of the interacting components of the system, while macroscopic quantities are obtained by suitable moments weighted by the above distribution function.

Both observation and simulation of system of real world need the definition of suitable observation and modeling scales. Different models and descriptions may correspond to different scales. For instance, if the motion of a fluid in a duct is observed at a microscopic scale, each particle is singularly observed. Consequently the motion can be described within the framework of Newtonian mechanics, namely by ordinary differential equations which relate the force applied to each particle to its mass times acceleration. Applied forces are generated by the external field and by interactions with the other particles.

On the other hand, the same system can be observed and described at a larger scale considering suitable averages of the mechanical quantities linked to a large number of particles, the model refers to macroscopic quantities such as mass density and velocity of the fluid. A similar definition can be given for the mass velocity, namely the ratio between the momentum of the particles in the reference volume and their mass. Both quantities can be measured by suitable experimental devices operating at a scale of a greater order than the one of the single particle. This class of models is generally stated by partial differential equations.

Actually, the definition of *small* or *large* scale has a meaning which has to be related to the size of the object and of the volume containing them. For instance, a planet observed as a rigid homogeneous whole is a single object which is small with respect to the galaxy containing the planet, but large with respect to the particles constituting its matter. So that the galaxy can be regarded as a system of a large number of planets, or as a fluid where distances between planets are neglected with respect to the size of the galaxy. Bearing all above in mind, the following definitions are given:

Microscopic scale

A real system can be observed, measured, and modeled at the microscopic scale if all single objects composing the system are individually considered, each as a whole.

Macroscopic scale

A real system can be observed, measured, and modeled at the macroscopic scale if suitable averaged quantities related to the physical state of the objects composing the system are considered.

Mesoscopic scale

A real system can be observed, measured, and modeled at the mesoscopic (kinetic) scale if it is composed by a large number of interacting objects and the macroscopic observable quantities related to the system can be recovered from moments weighted by the distribution function of the state of the system.

As already mentioned, microscopic models are generally stated in terms of ordinary differential equations, while macroscopic models are generally stated in terms of partial differential equations. In all cases they will generally be developed, unless otherwise specified, within the framework of deterministic causality principles. This means that once a cause is given, the effect is deterministically identified, however, even in the case of deterministic behavior, the measurement of quantities needed to assess the model or the mathematical problem may be affected by errors and uncertainty.

1.3. Dimensional Analysis for Mathematical Models

Frequently it is very conveniently to pass to the "dimensionless" form of equations. Parameters of dimensionless system of the equations usually represent some complexes describing dynamics of system and type of its behaviour (for example, as Reynolds number).This procedure should be generally, may be always, applied. In fact, it is always useful, and in some cases necessary, to write models with all independent and dependent variables written in a dimensionless form by referring them to suitable reference variables. These should be properly chosen in a way that the new variables take value in the domains $[1,1]$ or $[-1,1]$.

The above reference variables can be selected by geometrical and/or physical arguments related to the particular system which is modeled. Technically, let w_v be a certain variable (either independent or dependent), and suppose that the smallest and largest value of w_v, respectively w_m and w_M, are identified by geometrical or physical measurements; then the dimensionless variable is obtained as follows:

$$w = \frac{w_v - w_m}{w_M - w_m}, \quad w \in [0,1].$$

In principle, the description of the model should define the evolution within the domain $w \in [0,1]$. When this does not occur, then the model should be critically analyzed. If w_v corresponds to one of the independent space variables, say it correspond to x_v, y_v and z_v for a system with finite dimension, then the said variable can be referred to the smallest and to the largest values of each variable in a similar way. In some cases, it may be useful referring all variables with respect to only one space variable, generally the largest one.

Some words more on the (more delicate) choice of the reference time. Technically, if the initial time is t_0 and t_v is the real time, one may use the following:

$$t = \frac{t_v - t_0}{T_c - t_0}, \quad t \geq 0.$$

where generally one may have $t_0 = 0$. The choice of T_c has to be related to the actual analytic structure of the model and some characteristic features of the (physical) process.

1.4. Classiffcation of Models and Problems

The above sections have shown that the observation and representation at the microscopic scale generates a class of models stated in terms of ordinary differential equations, while the macroscopic representation generates a class of models stated in terms of partial differential equations. In details, the following definitions can be given:

Dynamic and static models

A mathematical model is dynamic if the state variable u depends on the time variable t. Otherwise the mathematical model is static.

Finite and continuous models

A mathematical model is finite if the state variable does not depend on the space variables. Otherwise the mathematical model is continuous.

A conceivable (and very relative) classification can be related to the above definitions and to the structure of the *state variable*, as it is shown in the following table:

finite	static	$\mathbf{u} = \mathbf{u}_e$
finite	dynamic	$\mathbf{u} = \mathbf{u}(t)$
continuous	static	$\mathbf{u} = \mathbf{u}(\mathbf{x})$
continuous	dynamic	$\mathbf{u} = \mathbf{u}(t, \mathbf{x})$

Figure 1.4.1. Classification of mathematical models

The above classification corresponds to well defined classes of equations. Specifically:

- *finite dynamic models* correspond to *ordinary differential equations*;
- *continuous dynamic models* correspond to *partial differential equations*.

Static models, both finite and continuous, have to be regarded as particular cases of the corresponding dynamic models obtained equating to zero the time derivative. Therefore:

- *finite static models* correspond to *algebraic equations*;
- *continuous static models* correspond to *partial differential equations* with partial derivatives with respect to the space variables only.

1.5. Critical Analysis

Previous part of the text has been proposed as an introduction to modeling, classification and organization of mathematical models and equations. It has been stated that a deeper insight into mathematical aspects can be effectively developed only if a well defined class of models (and equations) is effectively specialized. Lets discuss some ideas concerning *model validation* and *complexity problems in modeling*.

Referring to *model validation* one can state, in general, that a model can be regarded *valid* if it is able to provide information on the evolution of a real system sufficiently near to those obtained by experiments on the real system. So far a conceivable modeling procedure needs the development of the following steps:

- The real system is modeled by suitable evolution equations able to describe the evolution of the dependent variables with respect to the independent ones.
- Mathematical problems are generated by linking to the model all conditions necessary for its solution. These conditions should be generated by experimental measurements on the real system.
- The above problems can be possibly solved and the output of the simulations is compared with the experimental observations.
- If the distance (according to a concept to be properly defined in mathematical terms) between the above simulations and experiments is less than a critical value fixed *a priori*, then the model can be regarded valid, otherwise revisions and improvements are necessary.

Unfortunately, the concept of validity is not universal, but it refers to the circumstances related to the above comparisons. Indeed, a model which is valid to describe certain phenomena, may loose validity with reference to different phenomena. Therefore development of models and their application needs a constant critical analysis which can go on following a systematic analysis and improvements of each model.

Referring now to *complexity problems in modeling*, it is worth stating that this concept can be applied to the real system, as well as to the model and to the mathematical problems. In principle all systems of the real world are complex, considering that the number of real variables suitable to describe each system may be extremely large, if not infinite. Once applied mathematicians try to constrain the real system into a mathematical model, i.e. into a mathematical equation, then a selection of the variables suitable to describe the state of the real system is done.

In other words, every model reduces the complexity of the real system through a simplified description by a finite number of variables. Enlarging the number of variables makes the model virtually closer to the real system.

On the other hand this enlargement may cause complexity in modeling. In fact a large number of variables may need experiments to identify the phenomenological models related to the material behavior of the system, which may require high costs to be realized, and, in some cases, may be impossible.

However, suppose that the applied mathematician is able to design a model by a large number of variables, then the related mathematical problem may become too difficult to be dealt with. Technically, it may happen that the computational time to obtain a careful solution increases exponentially with the number of variables. In some cases, mathematics may not even be able to solve the above problems. The above concepts refer to *complexity related to mathematical problems*. Once more, this is a critical aspects of modeling which involves a continuous intellectual effort of applied mathematicians.

It is plain that the attempt to reduce complexity may fall in contrast with the needs posed by validation. Let us anticipate some concepts related to *validation of models*. Essentially, a validation process consists in the comparison between the prediction delivered by the model and some experimental data available upon observation and measurement of the real system. If this distance is \small", then one may say that the model is valid. Otherwise it is not.

The above distance can be computed by a suitable norm of the difference between the variable which defines the state of the model and the measurement obtained on the real system related to the same variable. Of course, different norms have to be used according to the different classes of models in connection to the different representation scales.

Let us critically focus on some aspects of the validation problems and their interplay with complexity problems:

- The validation of a model is related to certain experiments. Hence a validity statement holds only in the case of the phenomena related to the experiment. In different physical conditions, the model may become not valid.
- The evaluation of the distance between theoretical prediction and measurements needs the selection of a certain norm which needs to be consistent not only with the analytic structure of the model, but also with the data available by the measurements.
- The concept of *small* and *large* related to the evaluation of the deviations of the theoretical prediction from the experimental data has to be related both to the size (in a suitable norm) of the data, and to the type of approximation needed by the application of the model to the analysis of real phenomena.
- Improving the accuracy (validity) of a model may be contrasted by the complexity problems concerning both modeling and simulations. In some cases accuracy may be completely lost due to errors related to complex computational problems

Mathematical modeling constantly supports the development of applied sciences with the essential contribution of mathematical methods. In the past centuries, a systematic use of modeling methods have generated classical equations of mathematical physics, namely equations describing hydrodynamics, elasticity, electromagnetic phenomena etc. Nowadays, modeling refers to complex systems and phenomena to contribute to the development of technological sciences.

Mathematical models already contribute, and in perspective will be used more and more, to the development of sciences directly related to quality of life, say, among others, biology, medicine, earth sciences.

Modelling processes are developed through well defined methods so that it is correct to talk about the *science of mathematical modelling*. The first stage of this complex process is the observation of the physical system which has to be modelled. Observation also means organization of experiments suitable to provide quantitative information on the real system. Then a mathematical model is generated by proper methods to deal with mathematical methods.

Generally a mathematical model is an evolution equation which can potentially describe the evolution of some selected aspects of the real system.

The description is obtained solving mathematical problems generated by the application of the model to the description of real physical behaviors. After simulations it is necessary to go back to *experiments* to validate the model. As we shall see, problems are obtained linking the evolution equation to the so-called *initial and/or boundary conditions*. Indeed, the simplest differential model cannot predict the future if its behavior in the past and on the boundaries of the system are not defined.

In summary we will quote the well-known statement ("the basic thesis of a method of mathematical modelling") that "there is no best model, only better models".

There exist a lot of diagrams, which shows the essence (the basic idea) of the method of mathematical modelling.Below we show for an illustration some of them. Clearly, that is possible to repeat again the above mentioned basic thesis of a method of mathematical modelling – this time, certainly, it will be connected with those diagrams – "there is no best diagram, only better diagrams".

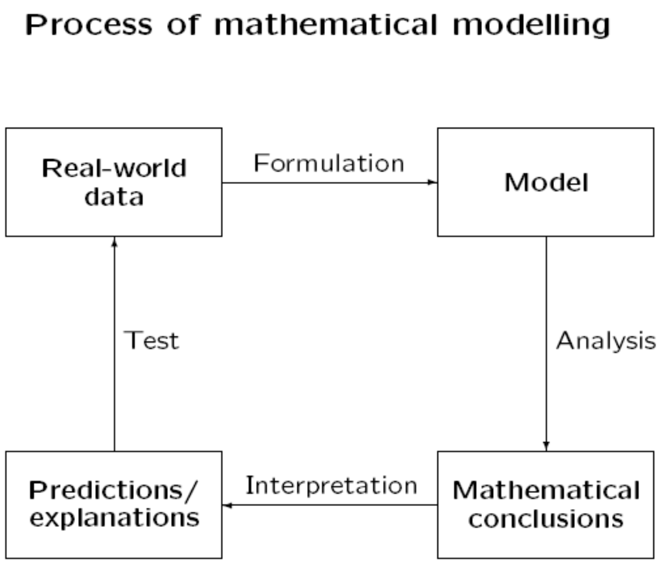

Figure 1.5.1. Process of mathematical modelling

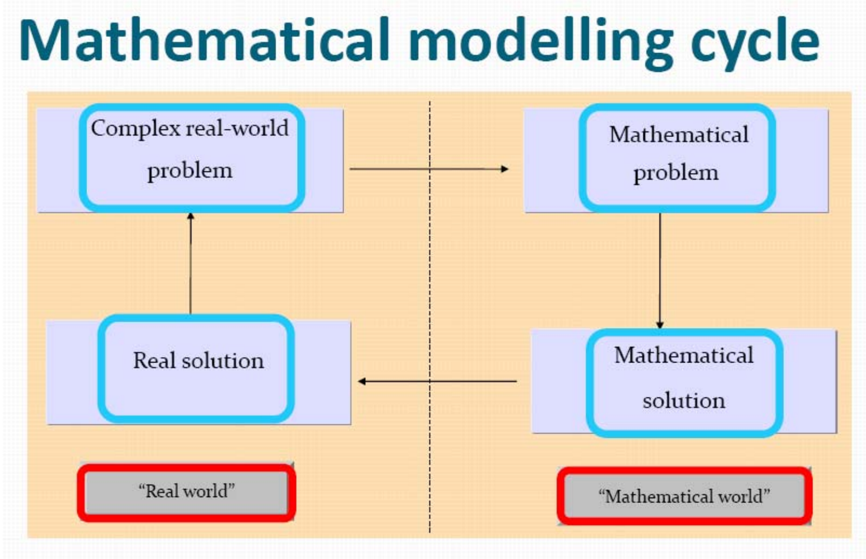

Figure 1.5.2. Mathematical modelling cycle

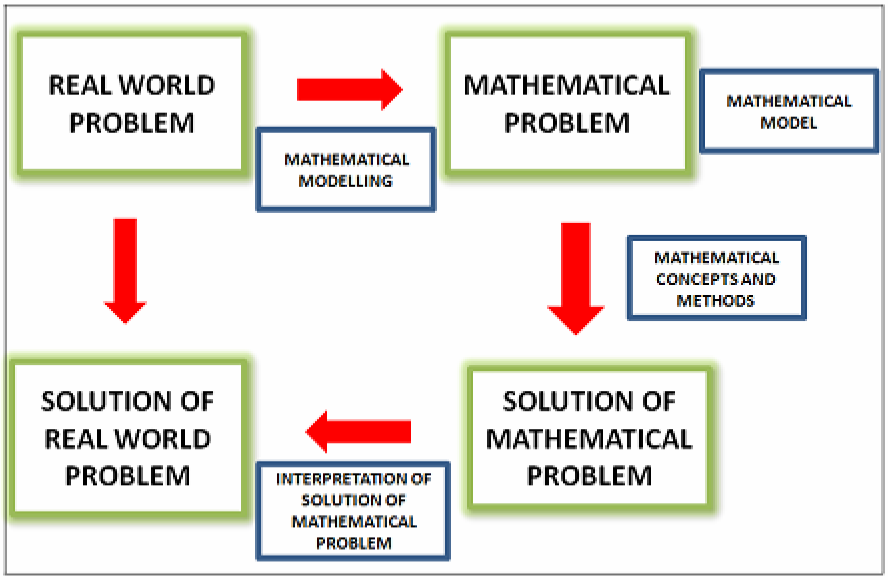

Figure 1.5.3. Methodology of Solution of real world problems[3]

Many other similar illustrations may be found in different books and in the materials in Internet. Figures 1.5.1 – 1.5.3 represens the essence of a such diagrams.

Below one more similar diagram will be showed – at this time it will show in details the basic stages of the method of mathematical modelling – so to say, in technological (practical) aspect.

[3] See, for example, Milanovic I., Vukobratovic R., Raicevic V., An instance of a mathematical model in chemical kinetics // *Int. J. Knowledge Engineering and Soft Data Paradigms*. 2012. Vol. 3, Nos. ¾. P. 294–308; P.299

Unit 2. Some technological details of the Mathematical Modelling

2.1. The General purposes of the Method of Mathematical Modelling. Statements and formulations of classics

In order to explain once more the purpose of modelling, it is helpful to start by asking: what is a mathematical model? One answer was given by Rutherford Aris [Aris R., 1994]:

"*A model is a set of mathematical equations that … provide an adequate description of a physical system*".

Dissecting the words in his description, "*a physical system*" can be broadly interpreted as any real-world problem – natural or man-made, discrete or continuous and can be deterministic, chaotic, or random in behaviour. The context of the system could be physical, chemical, biological, social, economic or any other setting that provides observed data or phenomena that we would like to quantify. Being "*adequate*" sometimes suggests having a minimal level of quality, but in the context of modelling it describes equations that are good enough to provide sufficiently accurate predictions of the properties of interest in the system without being too difficult to evaluate.

Trying to include every possible real-world effect could make for a complete description but one whose mathematical form would likely be intractable to solve. Likewise, over-simplified provide accurate descriptions of the original problem. In this spirit, Albert Einstein supposedly said, "Everything should be made as simple as possible, but not simpler" [Einstein A., 2015], though ironically this is actually an approximation of his precise statement [Einstein A., 1934].

Many scientists have expressed views that systems may become mathematically trivial and will not be the subject of modelling. But in general expressed views about the importance of modelling and the limitations of models. Some other notable examples are:

- In the opening of his foundational paper on developmental biology, Alan Turing wrote "This [mathematical] model will be a simplification and an idealisation, and consequently a falsification. It is to be hoped that the features retained for discussion are those of greatest importance …" [Turing A.M., 1952].
- George Box wrote "…all models are wrong, but some are useful" [Box G.E.P., Draper N.R., 1987].
- Mark Kac wrote "Models are, for the most part, caricatures of reality, but if they are good, they portray some features of the real world" [Kac M., 1969].

Useful models strike a balance between such extremes and provide valuable insight into phenomena through mathematical analysis. Every proposed model for a problem should include a description of how results will be obtained – a solution strategy. This suggests an *operational definition*:

Model: a useful, practical description of a real-world problem, capable of providing systematic mathematical predictions of selected properties.

Models allow researchers to assess balances and trade-offs in terms of levels of calculational details versus limitations on predictive capabilities.

Concerns about models being "wrong" or "false" or "incomplete" are actually criticisms of the levels of physics, chemistry or other scientific details being included or omitted from the mathematical formulation. Once a well-defined mathematical problem is set up, its mathematical study can be an important step in understanding the original problem. This is particularly true if the model predicts the observed behaviours (a positive result). However, even when the model does not work as expected (a negative result), it can lead to a better understanding of which (included or omitted) effects have significant influence on the system's behaviour and how to further improve the accuracy of the model.

While being mindful of the possible weaknesses, the positive aspects of models should be praised,

Models are expressions of the hope that aspects of complicated systems can be described by simpler underlying mathematical forms.

Exact solutions can be found for only a very small number of types of problems; seeking to extend systems beyond those special cases often makes the exact solutions unusable. Modelling can provide more viable and robust approaches, even though they may start from counterintuitive ideas, "*… simple, approximate solutions are more useful than complex exact solutions*" [Borwein J.M., Crandall R.E., 2013].

Amazingly, but many – many years prior to this statement the similar reason was stated by the well-known Ukrainian educator and philosopher Grigory Savvich Skovoroda (22.11 (03.12). 1722 – 29.10 (09.10). 1794): «the God has created the world so, that everything, that is necessary, not so difficultly, and, that is difficult, not so necessary»[4].

Mathematical models also allow for the exploration of conjectures and hypothetical situations that cannot normally be de-coupled or for parameter ranges that might not be easily accessible experimentally or computationally. Modelling lets us qualitatively and quantitatively dissect problems in order to evaluate the importance of their various parts, which can lead to the original motivating problem becoming a building block for the understanding of more complex systems. Good

[4] Григорий Саввич Сковорода (22.11(03.12).1722 – 29.10(09.10).1794): «Бог создал мир так, что все, что нужно, не очень сложно, а все, что сложно, не очень нужно».

models provide the flexibility to be systematically developed allowing more accurate answers to be obtained by solving extensions of the model's mathematical equations. In summary, our description of the process is

Modelling: a systematic mathematical approach to formulation, simplification and understanding of behaviours and trends in problems.

2.2. Levels of Models

Mathematical models can take many different forms spanning a wide range of types and complexity,

"*Toy*" problems $\leq$ Math Models $\leq$ Complete systems

At the upper end of complexity are models that are equivalent to the full first-principles scientific description of all of the details involved in the entire problem. Such systems may consist of dozens or even hundreds of equations describing different parts of the problem; computationally intensive numerical simulations are often necessary to investigate the full system.

At the other end of the spectrum are improvised or phenomenological "*toy*" Problems (which sometimes also described as ad hoc or heuristic models.) that may have some conceptual resemblance to the original system but have no obvious direct derivation from that problem. These might be only a few equations or just some geometric relations. They are the mathematical modelling equivalents of an "artistic impression" motivated or inspired by the original problem. Their value is that they may provide a simple "proof of concept" prototype for how to describe a key element of the complete system. As rule, heuristic models also describes (differentiate) at a qualitative level the possible (probable) and impossible phenomena (within the framework of the accepted and obviously formulated assumptions).

Both extremes have drawbacks: intractable calculations in one extreme, and imprecise qualitative results at the other. Mathematical models exist in-between and try to bridge the gap by offering a process for using identifiable assumptions to reduce the full system down to a simpler form, where analysis, calculations and insights are more achievable, but without losing the accuracy of the results and the connection to the original problem.

2.3. Classes of Real World Problems

The kinds of questions being considered play an important role in how the model for the problem should be constructed. There are three broad types of questions:

- Evaluation questions [also called Forward problems]: Given all needed information about the system, can we quantitatively predict its other properties and how the system will function?
- Detection questions [Inverse problems] [Banks H.T., Tran T.H., 2009]: If some information about a "black box" system is not directly available, can you "reverse engineer" those missing parameters?
- Design questions [Control and optimisation problems]: Can we create a solution that best meets a proposed goal?

There are many routes available to attack such questions that are typically treated in different areas of study. In this book we will present some methods for the research some problems of the first type of problems in the context of continuous systems and differential equations.

2.4. Stages of the Modeling Process

The modeling process can sometimes start from some toy problem and then seeks to validate the model's connection to the original problem. However, this approach requires having a lot of previous experience with and background knowledge on the scientific area and/or relevant mathematical techniques in order to generate the new model. Many books offer the more formal schemes and the more systematic approach of starting with some version of the complete scientific problem statement and then using mathematical techniques to obtain reduced models that can be simplified to a manageable level of computational difficulty.

The modeling process has two stages, consisting of setting up the problem and then solving it:

- **Formulation phase**. In this phase, the problem is described using basic principles or governing laws and assumed relations taken from some branches of knowledge, such as physics, biology, chemistry, economics, geometry, probability or others. Then all side-conditions that are needed to completely define the problem must be identified: geometric constraints, initial conditions, material properties, boundary conditions and design parameter values. Finally, the properties of interest, how they are to be measured, relevant variables, coordinate systems and a system of units must all be decided on.
- **Solution phase**. This phase is implemented under the assumption that the problem cannot be easily solved analytically or computed numerically, and hence does not need modeling. In this solution phase, mathematical modeling provides approaches to reformulating the original problem into a more convenient structure from which it can be reduced into solvable parts that can ultimately be re-assembled to address the main questions of interest for the problem.

In some cases, the reformulated problem may seem to only differ from the original system at a notational level, but these changes can be essential for separating out different effects in the system. At the simplest level, “problem reduction” consists of obtaining so-called asymptotic approximations of the solution, but for more challenging problems, this will also involve approaches for transforming the problem into different forms that are more tractable for analysis or computation.

The techniques described here are broadly applicable to many branches of engineering and applied science: biology, chemistry, physics, the geosciences and mechanical engineering, to name a few. We direct interested readers to books that present more detailed case studies of such problems in specific application areas. The above-mentioned two-step simulations are usually divided into several smaller sub-steps. We have already mentioned the various diagrams describing the modeling (figures 1.5.1 – 1.5.3 represent the essence of a such diagrams). The more detailed modeling process is best illustrated in the following diagrammatic form[5] (see fig. 2.4.1).

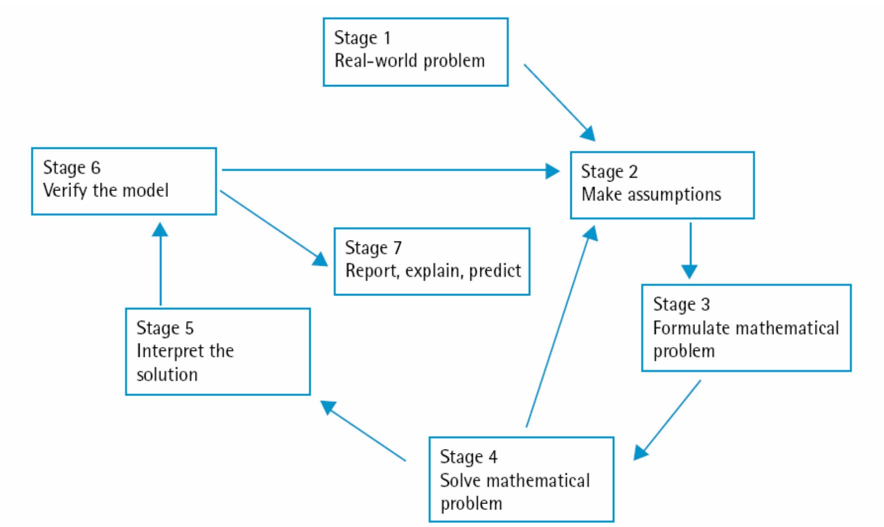

Figure 2.4.1. The more detailed modeling process – technological (practical) aspect

The modelling process

Stage 1: Real-world problem

The problem statement should be very general and free of as much data as possible, as later stages of the modeling process will consider and gather what is

[5] More in detail about this concept and its appendices see in Mathematical modeling and the general mathematics syllabus. NSW Department of Education and Training. University of Western Sydney. http://www.curriculumsupport.education.nsw.gov.au/secondary/mathematics/assets/pdf/s6_teach_ideas/cs_articles_s6/cs_model_s6.pdf Accessed 02.04.2016.

needed. Often teachers will have to rewrite a typical textbook problem to reduce the initial information included.

Stage 2: Make assumptions

This is the most valuable part of the process and it should not be rushed. It consists of listing all the variables involved and then trying to simplify or modify the list. In this process, it becomes obvious that there is a need to obtain certain information that will constitute the initial conditions of the problem.

Stage 3: Formulate mathematical problem

The choice of mathematical model will depend upon the approach used by the teacher and the demands of the syllabus. If the class decides upon a model that does not match the teacher's, then the teacher has a choice to either intervene (a structured approach) or to delay until the completion of one cycle of the modeling process. The teacher has the option of algebraically constructing the model with the class or providing a spreadsheet containing the model.

Stage 4: Solve the mathematical problem

This stage describes the process used by the students when applying a procedure to given data. Using the modeling process may mean a return to the initial assumptions in order to modify the problem being considered.

Stage 5: Interpret the solution

After obtaining their solutions, the students are directed back to the problem. They must check to ensure that they have answered the problem within the assumptions they have made. Interpretations made should make explicit the assumptions and initial conditions. This is an important step in helping students realise that solutions to problems are constrained by the context and are not easily transferable to other situations.

Stage 6: Verify the model

In this stage the strengths and weaknesses of the model are discussed. This involves reflecting upon the mathematics that has been used. The statement that "all models are wrong, but some are useful" is an important reminder of the dangers of oversimplification and of ignoring the underlying assumptions. Models should be evaluated in terms of the variables used and, more importantly, those omitted.

Stage 7: Report, explain, predict

This is a valuable part of the process, as students need experience in using language to express mathematical ideas. It is here that we reflect upon the quality of the students' thinking. It should include documentation of the students' progress through the stages of the cycle as well as their final predictions and answers. The structure of the modeling process provides a good organizing device for their report.

Unit 3. Continuous Population Models for Single Species

3.1. Probably the first and maybe the simplest mathematical model of dynamics of biological populations is a well-known model, built in 1202 by the famous Italian mathematician Leonardo from Pisa (Fibonacci)[6]. It is believed that he was one of the most talented Italian mathematicians of the middle ages. Fibonacci played a prominent role in the transition of Europe to the decimal system and use of Arabic numerals. Particularly significant role in this process belongs to his work "Liber Abaci", in which in addition to the examples of the practical use of new computing technology, made noticeable contribution in bookkeeping and accounting, calculate interests, transfer from one unit to another of weights and measures and other "commercial" applications of mathematics. The book contains the formulation and the solution of (highly idealized) problem about the growth of a hypothetical population of the rabbits, in which the author introduced some sequence of integers, now known as the Fibonacci numbers[7].

His father Guglielmo – the official of city of Pisa and famous trader (wholesale dealer), was appointed customs official the Borgias in North Africa. He directed that his son joined to him as assistant, and also for the purpose of completing his education. Leonardo began to make numerous business trips to the Mediterranean territory. Probably it is the latter explains the interest of Fibonacci to "economic" applications of mathematics. Anyway, it had known the work "Liber Abaci" was published after one of the journeys Fibonacci in Egypt.

In addition to the "Liber Abaci", Leonardo Fibonacci wrote two outstanding mathematical work: "Practica Geometricae" (1220), sacred geometry and trigonometry, and "Liber Quadratorum", dedicated to the theory of Diophantine equations.

In the Fibonacci's book "Liber Abaci" ("Book about Abaca", or "the Book about the computations"), which second edition of 1228 year survived until the new time, contains the problem which can be formulated in the following way:

"*How many pairs of rabbits are born in one year from one pair, if the nature of rabbits is such that after the month a pair of rabbits give birth to another couple, and give birth to rabbits from the second month after their birth*?"

In this model the population, elements of which primary were the pair of rabbits (not individuals); thus, the population is subdivided into two groups (or subpopulations) of young and adult rabbits; these groups are characterized by their ability to produce offspring. Another interesting feature of this model – the age of individuals can take two values ("young" or "adult"). In this system those two

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[6] Leonardo Pisano Fibonacci (1170 – 1250), or Leonardo Fibonacci, or simply Fibonacci.

[7] However, this sequence was long before that (not later than the VI century) already known to Indian mathematicians

subpopulations coexists. It is interesting to note that the similar scheme of describing of the life cycle of "representative economic agent" may be found in the models with discrete time in the theory of economic growth ("the overlapping generations model", or "Overlapping Generation Models", "OLG – Models").

Lets choose in this problem as a time unit one month, and let us denote N_t the current population size (i.e. the number of pairs of rabbits) at the time $t \in \mathbf{Z}$, where $\mathbf{Z}$ is the set of integers. Then, in accordance with the definition, the following relation is true:

$$N_t = N_{t-1} + N_{t-2}\,,\ t \ge t_0 + 2\,. \tag{3.1}$$

Here t_0 – initial value of time. Relation (3.1) is the difference (differential-difference, recurrent) the equation describing the dynamics of this population. Note that since the problem was formulated to a very short period of time, then the equation (3.1) does not take into account the mortality of rabbits, so that, in a certain sense, the rabbits in Fibonacci immortal.

In order to determinate the unique solution of this problem (dynamics of this population) – that is, in order to uniquely define all elements of sequence $\{N_t, t \in \mathbf{Z}_{t_0}\}$, $\mathbf{Z}_{t_0} \equiv \{t_0, t_0+1, t_0+2, \ldots\}$ – it is necessary to specify initial conditions

$$N_{t_0} = 1, \quad N_{t_0+1} = 1\,, \tag{3.2}$$

It is easy to check that the first elements of this sequence are the following numbers:

$$1,\ 1,\ 2,\ 3,\ 5,\ 8,\ 13,\ 21,\ 34,\ 55,\ 89,\ 144,\ 233,\ 377, \ldots\,. \tag{3.3}$$

Numeric sequence (3.3) is called "a sequence of Fibonacci", and its elements – "the Fibonacci numbers". For Fibonacci numbers are often used the designation $\{F_n, n \in \mathbf{N}\}$, where $\mathbf{N} = \{1,2,3,\ldots\}$ is the set of natural numbers.

Initial problem (3.1), (3.2) can be easily solved using standard methods (see, e.g., [Ferguson B. S., Lim G. C., 2003]); like every sequence defined by a linear recurrence with constant coefficients, the Fibonacci numbers have a closed-form solution. It has become known as "Binet's formula", even though it was already known by Abraham de Moivre[8]. This representation for the Fibonacci numbers is given by:

$$F_n = \frac{A^n - B^n}{\sqrt{5}}\,, \qquad n \in \mathbf{N}\,, \tag{3.4}$$

[8] See, for example, https://en.wikipedia.org/wiki/Fibonacci_number Accessed 04.03.2016

where $A = (1+\sqrt{5})/2 \approx 1{,}618$, $B = (1-\sqrt{5})/2 \approx -0{,}618$. However, the validity of the representation (3.4) can easily justify also using the method of mathematical induction.

From the representation (3.4) it follows that the Fibonacci number F_n is the nearest next integer to the n - th element A_n of a geometric progression, the first element of which is $A/\sqrt{5}$ and the denominator is equals to A, so

$$F_n \approx A_n = \frac{1}{\sqrt{5}} A^n \quad , \; n \in \mathbf{N} .$$

It is clear, that we have the following approximate representation

$$F_n \approx AF_{n-1}, \quad A = const \approx 1{,}618, \quad n \in \mathbf{N} . \tag{3.5}$$

The Fibonacci numbers have some very interesting properties and find applications in several branches of mathematics and its applications, for example, in the theory of chain (continuous fractions) and in the theory of optimal control.

If we talk about models of population dynamics of populations, the next time of its appearance was on the turn of XVIII and XIX centuries the model of Thomas Robert Malthus (1766 – 1834). This model was published in 1798 and has gained very wide popularity.

It is interesting to note that in 1805 Malthus was appointed professor of modern history and political economy of the College of Eastern India (East India College, Haileybury), and thus it becomes the first "academic economist" of England.

The logic of the reasoning and conclusions of the works of Malthus T.R. is approximately as follows. Due to the biological characteristics of human population tends to increase exponentially according to the law (cp. (3.5))

$$N_n = MN_{n-1} \;, \; n \in \mathbf{N} , \tag{3.6}$$

where $M > 1$ is the denominator is a geometric progression. Thus, $N_n = M^n N_0$, $n \in \mathbf{N}$. At the same time means of existence being increased by the law of arithmetical progression, so

$$C_n = C_{n-1} + D , \; D > 0 , \; n \in \mathbf{N} . \tag{3.7}$$

It is clear that $C_n = C_0 + nD$.

The comparison of (3.6) and (3.7) shows that the amount of funds of existence per capita (per capita) – “consumption” – changing in accordance with the formula

$$c_n = \frac{C_0 + nD}{M^n N_0} , \; M > 1 \; , \; n \in \mathbf{N} . \tag{3.8}$$

So, from (1.8) t follows immediately that $c_n \to 0$, $n \to \infty$.

On the basis of this result, Malthus predicted rapid lagging agricultural production to the needs of the rapidly growing population. Here is a quote:

> "*Taking the population of the world at any number, a thousand millions, for instance, … , the human species would increase in the ratio of* 1, 2, 4, 8, 16, 32, 64, 128, 256, 512, *etc. and subsistence* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, *etc. In two centuries the population would be to the means of subsistence as* 512 *to* 10; *in three centuries as* 4096 *to* 13, *and in two thousand years the difference would be incalculable.*"

However, this prediction turned out to be wrong, and about 200 years after this prediction food production per capita has continued to grow. This process is halted only in the 80s of the twentieth century

Despite the above the folly of his forecast , Malthus was right in the other – they were first formulated quite sober the idea that people's needs must be consistent with the real possibilities of production and Nature. This idea would, however, formulated in a very provocative form:

"What enlightened classes in their desire to ensure the overall well-being, if the lower classes will continue to multiply like rabbits?"

This statement has caused a public outcry, and the terms "Malthusian" and "Malthusianism" came to be regarded almost as a curse.

Nevertheless, it is necessary to note the undoubted merit of an Anglican pastor in the formulation of the question of the reasonableness of the development of European civilization on the basis of classical rationalism and the principle of "conquering nature".

Only 200 years later, in 1992, at the International Ecological Congress in Rio de Janeiro at the level of Heads of Government was proclaimed the principle of "sustainable development", affirming the inadmissibility of the unlimited and uncontrolled use of resources and pollution of the biosphere. Despite the criticisms of declarative and streamlining of the Congress decisions, as important as the fact of reviewing the approach to the development of civilization, and the wording of the total for the entire planet's development strategy.

Let us return to the construction of a general model of "Malthusian type" of dynamics of population growth. Disregard of the internal characteristics of individuals - members of the population - and we will consider only the two "basic" processes which are characteristics of the biological nature of the population. This process of birth and death (mortality). The population is characterized by its strength $N(t)$ at time $t \in \mathbf{R}_{t_0} \equiv [t_0, \infty)$.

For output equations of dynamics let us consider "the balance of births and deaths" for some period of time $[t, t+\Delta t]$. By definition, the change $\Delta_t N$ in the function $N(t)$ will be

$$\Delta_t N \equiv N(t+\Delta t) - N(t)\,. \tag{3.9}$$

On the other hand, this change is determined by the processes of birth and death of individuals. It is natural to assume that quantity of acts of births (deaths) is greater for the longer the period of time and for the greater number of the population. Assume that both these processes are characterized by some functions and $B(N,t)$ and $D(N,t)$ (fertility function and mortality function, respectively) so that the number of births $\Delta_t B$ and deaths $\Delta_t D$ of individuals for the period of time $[t, t+\Delta t]$ are, respectively,

$$\Delta_t B = B(N,t)N(t)\Delta t + o_B(\Delta t)\,,\ \Delta_t D = D(N,t)N(t)\Delta t + o_D(\Delta t)\,, \tag{3.10}$$

where $\dfrac{o_p(\Delta t)}{\Delta t} \to 0$, $\Delta t \to 0$, $p = B, D$.

In accordance with the biological sense of parameters, $\Delta_t N = \Delta_t B - \Delta_t D$, and it follows from (3.9) and (3.10) that we have the relation

$$N(t+\Delta t) - N(t) = \{B(N,t) - D(N,t)\}N(t)\Delta t + o(\Delta t)\,. \tag{3.11}$$

From (3.11) when we get the differential equation

$$\frac{dN(t)}{dt} = \{B(N,t) - D(N,t)\}N(t)\,,\ t \in \mathbf{R}_{t_0} \equiv [t_0, \infty)\,. \tag{3.12}$$

The function $M(N,t) \equiv B(N,t) - D(N,t)$ is usually called the Malthusian function. The following initial condition must be added to the equation (3.12)

$$N(t)\big|_{t=t_0+0} = N_0 > 0\,. \tag{3.13}$$

A property of populations identified by T. Malthus can be described as follows. Let the functions of fertility and mortality are constant values $B(N,t) = b > 0$ and $D(N,t) = d > 0$ respectively. Then the equation (3.12) can be written in the form

$$\frac{dN(t)}{dt} = rN(t)\,,\ t \in \mathbf{R}_{t_0} \equiv [t_0, \infty)\,, \tag{3.14}$$

where $r \equiv b - d > 0$ – *Malthusian parameter*. Equations (3.14), (3.13) implies that the population size is described by the formula

$$N(t) = N_0 e^{r(t-t_0)},\ t \in \mathbf{R}_{t_0} \equiv [t_0, \infty). \tag{3.15}$$

If we consider discrete time $t_n = t_0 + n\Delta t$, we obtain for $N_n = N(t_n)$:

$$N_n = N_0 \{e^{r\Delta t}\}^n \equiv N_0 \mu^n,\ \mu = e^{r\Delta t} > 1,\ n \in \mathbf{N}, \tag{3.16}$$

which corresponds to the concept of T. Malthus that population tends to increase according to the law of geometric progression.

3.2. Mathematical model (3.14) (further referred to as model of Malthus) reflects a very simplified picture of the dynamics of populations. Much more realism can be expected from the generalized models of the type (3.12). In models of this type as possible given the limited resources of the habitat of the populations, and the broad scope of the intraspecific interaction between individuals (in particular, intraspecific competition). Consider some of these models, not considering the possible dependence on time of the functions of fertility and mortality (and, consequently, Malthusian functions). In this case, equation (3.12) can be written in the form

$$\frac{dN(t)}{dt} = M[N(t)]N(t),\ t \in \mathbf{R}_{t_0} \equiv [t_0, \infty), \tag{3.17}$$

where $M(N) \equiv B(N) - D(N)$ – the Malthusian function. The initial condition (3.13) must be added to the equation (3.17)

At various times it has been proposed a number of expressions for Malthusian functions that provide a greater agreement between the theoretical results with experimental data. Apparently, the most popular form of today function goes back to the works of P.F. Verhulst (Pierre François Verhulst, 28. 10. 1804, Brussels, Belgium – 15.02. 1849, Brussels, Belgium) and usually dates back to 1838 year. However, these works were actually forgotten for a long time.

Only in the 1920s in the works of Pearl R. (Pearl, Raymond, 03.06.1879 - 17.11.1940) and Reed L.J., (Reed, Lowell J., 1886 - 1966) it was found that the population dynamics of many natural populations of a limited environment is really quite well described by "logistical dependence", which is consistent with the work of P. Verhulst. In the works of these authors is essentially proposed as follows Malthusian function

$$M_{VPR}(N) = r\left(1 - \frac{N}{K}\right),\quad r, K = const > 0. \tag{3.18}$$

Malthusian function (3.18) corresponds to the dynamics equation of the form

$$\frac{dN(t)}{dt} = r\left(1 - \frac{N(t)}{K}\right)N(t), \quad t \in \mathbf{R}_{t_0} \equiv [t_0, \infty), \tag{3.19}$$

which is usually called the equation of Verhulst - Pearl - Reed.

In (3.18), (3.19) the value $r > 0$ - analogue Malthusian parameter, and $K > 0$ - constant characterizing the habitat of the population.

Note that equation (3.19) can easily be obtained from (3.17) under the assumption of constant fertility function (so, $B(N) \equiv b$ where b – "natural fertility") and simple (linear) form of mortality function (so, $D(N) = m + \mu N$ where $m > 0$ - "natural mortality" and $\mu > 0$ - a parameter characterizing the mortality impact of the number (density) of the population, and it is easy to see that $r = b - m > 0$ and $K = \frac{r}{\mu} > 0$.

It is easy to establish that the solution of the problem (3.19), (3.13) is written as follows:

$$N(t) = \frac{N_0 e^{r(t-t_0)}}{1 + \frac{N_0}{K}[e^{r(t-t_0)} - 1]}, \; t \in \mathbf{R}_{t_0} \equiv [t_0, \infty). \tag{3.20}$$

From the elementary analysis of stability of equilibrium states of the equation (3.19) it easy obtain that the nontrivial equilibrium state $N_{st} = K$ is stable, and the trivial state $N_{st} = 0$ – is unstable (in the sense of Lyapunov A.M). It is obvious (in view of the representation (1.20)) that $N(t) \to K$ when $t \to \infty$; in such cases it is often talk about "saturation effect". Thus, the equilibrium state is asymptotically stable in the sense A.M. Lyapunov. Therefore, the parameter is the value of the equilibrium population size at which the population is able to exist in a given area "infinitely long" period of time. In other words, it is such a population size that this habitat may "feed" or "withstand". That is why the option is commonly referred to as the capacity of the habitat.

The curve described by (3.20) for $t \in \mathbf{R} = (-\infty, \infty)$, called "logistic curve" or "logistic dependence". It is clear that for any initial conditions $N_0 \in (0, K)$ the following inclusion has place $N(t) \in (0, K)$ for all, and $\frac{dN(t)}{dt} > 0$, $\forall t \in \mathbf{R}$. Using (3.19) is easily to calculate the second derivative $\frac{d^2N(t)}{dt^2}$, which has the form:

$$\frac{d^2N(t)}{dt^2} = rN(t)\left(1-\frac{N(t)}{K}\right)\left(1-\frac{2N(t)}{K}\right). \qquad (3.21)$$

It is clear that there exist such $t_{1/2}$ that the equality $N(t_{1/2}) = K/2$ take place, so that, as follows from (3.21),

$$\frac{d^2N(t)}{dt^2} = \begin{cases} > 0, & \text{при} \quad t < t_{1/2}, \\ = 0, & \text{при} \quad t = t_{1/2}, \\ < 0, & \text{при} \quad t > t_{1/2}, \end{cases} \qquad \left.\frac{dN(t)}{dt}\right|_{t=t_{1/2}} = \frac{rK}{4} > 0. \qquad (3.22)$$

Thus, by virtue of (3.22), for $t < t_{1/2}$ the logistic curve is convex, and when $t < t_{1/2}$ - concave. A point $t = t_{1/2}$ is a point of inflection. The general view of logistic curve is shown in Figure 3.1.

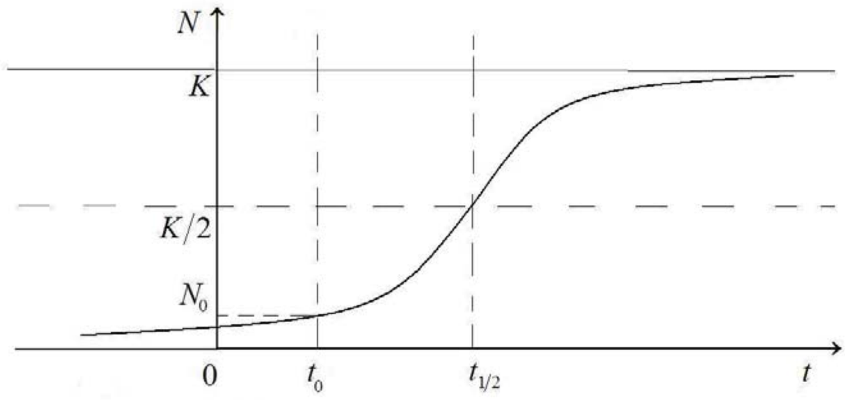


Figure 3.1. The qualitative form of logistic curve

Quantitative (in the broad sense) phenomenological theory of biological populations, growth and development should include the model and plant growth and development of organisms (as a specific form of cell populations). In addition to the representation (3.18) of Malthusian function $M(N)$ in the Verhulst - Pearl - Reed form there are many other, equally famous expressions, designed to give an adequate description of the growth and development of various biological structures. Here are some of them.

Malthusian function of Gompertz B. (1825)

$$M_G(N) = r\ln\left(\frac{K}{N}\right), \quad r, K = const > 0. \qquad (3.23)$$

and the equation of Gompertz B.. The last has the form:

$$\frac{dN(t)}{dt} = rN(t)\ln\left[\frac{K}{N(t)}\right], \ t \in \mathbf{R}_{t_0} \equiv [t_0, \infty) \ \text{ or} \tag{3.24}$$

$$\frac{d}{dt}\left[\frac{N(t)}{K}\right] = -r\left[\frac{N(t)}{K}\right]\ln\left[\frac{N(t)}{K}\right], \ t \in \mathbf{R}_{t_0} \equiv [t_0, \infty). \tag{3.25}$$

The solution of the problem (3.24), (3.25), (3.13) has the form:

$$N(t) = K\exp\left\{\ln\left(\frac{N_0}{K}\right)e^{-r(t-t_0)}\right\}, \ t \in \mathbf{R}_{t_0} \equiv [t_0, \infty). \tag{3.26}$$

From (3.26) it is clear, that $N(t) \to K$ when $t \to \infty$ (“saturation effect”).

Some another models. Model of Pütter A. (1920), Bertalanffy L., von (1960), Rosenzweig M. (1971) and Schoener N.W. (1972):

$$M_{PBRS}(N) = r\left[\left(\frac{K}{N}\right)^g - 1\right], \quad r, g, K = const > 0, \tag{3.27}$$

and the corresponding equation. The last has the form

$$\frac{dN(t)}{dt} = rN(t)\left\{\left[\frac{K}{N(t)}\right]^g - 1\right\}, \ t \in \mathbf{R}_{t_0} \equiv [t_0, \infty) \tag{3.28}$$

The solution of the problem (3.27), (3.28), (3.13) has the form:

$$N(t) = K\left\{1 + \left[\left(\frac{N_0}{K}\right)^g - 1\right]e^{-rg(t-t_0)}\right\}^{\frac{1}{g}}, \ t \in \mathbf{R}_{t_0} \equiv [t_0, \infty), \tag{3.29}$$

From (3.29) it is clear, that $N(t) \to K$ when $t \to \infty$ (“saturation effect”.).

Goel N.S., Maitra S.C., Montroll E.W. (1971):

$$M_{GMM}(N) = r\left[1 - \left(\frac{N}{K}\right)^b\right], \quad r, b, K = const > 0. \tag{3.30}$$

In this connection, it is natural to build general (in the mathematical sense) growth models. For example, in the works of Y.M. Svirezhev (see., e.g, [Svirezhev Yu.M., 1987, P.14]; see also [Svirezhev Yu.M., 1984] [Svirezhev Yu.M., 2008]) there was proposed the following generalization of the logistic model . We write down the model of the dynamics of the population size (3.17) in the form

$$\frac{dN(t)}{dt} = F[N(t)],\ t \in \mathbf{R}_{t_0} \equiv [t_0, \infty). \tag{3.31}$$

Let the function $F(\cdot): \mathbf{R}_+ \to \mathbf{R}$, $\mathbf{R}_+ \equiv [0, \infty)$ - a sufficiently smooth function (for example, class C^2). Then (3.31) is a generalized logistic (in the sense of Y.M. Svirezhev) if the following conditions are met:

- There exist $K \in (0, \infty)$ that $F(0) = F(K) = 0$;
- We have the following inequalities $F'(0) = r > 0$; $F'(N) < F'(0)$, $\forall N \in (0, \infty)$.

The population, which dynamics is described by the generalized logistic equation, called the generalized logistic population. The corresponding dynamics model may be called a generalized logistic model.

It is useful to check that the set of formulated above conditions holds for the equation (3.17) with the Malthusian type functions (3.19), (3.24), (3.25) and (3.28). A similar approach to that described for the construction of the common growth models presented in [Carrillo M., 2003].

Lets briefly describe the approach of[Carrillo M., 2003] of characterization of Sigmoidal Growth.

Growth is observed through the dynamic behavior of a particular variable, X, and the speed of growth can be measured through the growth rate of the variable, $\frac{dx}{dt}$, or alternatively through the relative growth rate, which takes the form $\frac{1}{x}\frac{dx}{dt}$. The simplest way to capture mathematically the dependence of the growth rate on the various social phenomena affecting the evolution of *X* is by means of an autonomous differential equation of the form

$$\frac{dx}{dt} = F(x) \tag{3.32}$$

that consequently will be used to describe a growth model. We will understand that a sigmoidal growth experiences two different phases, the first of which is characterized by an exponential growth, next followed by an asymptotic growth, in such a way that, finally, a *S*-shaped curve is described. These characteristics are translated into analytical properties in the following manner:

Definition: Given an increasing C^2 function $x(t)$, it is said to describe a sigmoidal growth if it has two horizontal asymptotes (upper and lower) and passes through a single point of inflection in its path.

We can assume, without loss of generality, that the lower asymptote will take the value $x = 0$, whereas the upper asymptote will be denoted by $x = L$.

Now, we would like to know what specific model could be associated to a sigmoidal growth variable, *x*.

Lets $F(x)$ has the following properties:

- $F(x)$ is a continuous and differentiable function.
- $F'(x) > 0$, since X is monotonously increasing.
- $F(x)$ presents a (single) maximum at the point x_i.
- $F(0) = 0$ and $F(L) = 0$ (because $\lim_{t\to\infty} x(t) = L$ and $\lim_{t\to-\infty} x(t) = 0$.
- The improper integrals
$$\int_0^{\varepsilon} \frac{1}{F(x)} dx \quad \text{and} \quad \int_{\mu}^{L} \frac{1}{F(x)} dx,\ \varepsilon, \mu \in (0, L),$$
are both divergent.

Then $x(t)$ describes a sigmoidal growth if and only if $x(t)$ solves the differential equation (3.32) with above mentioned properties.

It is easy to see that the approach works [Svirezhev Yu.M., 1987] and [Carrillo M., 2003] are very close.

Some problems for self study

Problem 1. Find the solution of the following initial-value problem for the equation of Verhulst – Pearl – Reed ("logistic equation"):

$$\frac{dN(t)}{dt} = r\left(1 - \frac{N(t)}{K}\right)N(t),\ t \in \mathbf{R}_{t_0} \equiv [t_0, \infty),$$
$$N(t)\big|_{t=t_0+0} = N_0 > 0.$$

Problem 2. Find the solution of the following initial-value problem for the equation of Gompertz:

$$\frac{dN(t)}{dt} = rN(t)\ln\left[\frac{K}{N(t)}\right],\ t \in \mathbf{R}_{t_0} \equiv [t_0, \infty),$$
$$N(t)\big|_{t=t_0+0} = N_0 > 0.$$

Problem 3. Find the solution of the following initial-value problem for the equation of Pütter A. – von Bertalanffy L. – Rosenzweig M. – Schoener N.W:

$$\frac{dN(t)}{dt} = rN(t)\left\{\left[\frac{K}{N(t)}\right]^g - 1\right\},\ t \in \mathbf{R}_{t_0} \equiv [t_0, \infty)$$

$$N(t)\big|_{t=t_0+0} = N_0 > 0 .$$

Problem 4. Find the solution of the following initial-value problem for the equation of Weibull W.:

$$\frac{dN(t)}{dt} = sa^{\frac{1}{s}}\left[\alpha - N(t)\right]\left\{\ln\left[\frac{\beta}{N(t)}\right]\right\}^{\frac{s-1}{s}} , \; t \in \mathbf{R}_{t_0} \equiv [t_0, \infty)$$

$$N(t)\big|_{t=t_0+0} = N_0 > 0 .$$

Problem 5. Many population models assume that an increase in population density has a negative effect on population growth. There is a class of population models, however, where an increase in population density stimulates population growth, especially at low population densities. This is called the Allee effect after the work of W.C. Allee in the nineteen thirties. A model that shows the Allee effect may have the following form.

$$\frac{dN}{dt} = rN\left(1 - \frac{N}{K} - \frac{a}{b+N}\right) \qquad (*)$$

for positive r, a, b, K . What are the equilibria and which are stable? How does the behaviour of solutions depend on the initial population density? How do you interpret the parameters in terms of population behaviour?

Unit 4. Discrete Population Models for Single Species

We have already met with this type of equation – difference equations – it was the equation associated with the Fibonacci problem.

4.1. Let us start with the basic properties of difference equations. It is sometimes more natural, when modeling the evolution of a population, to take into account not only the current situation, but also the past one: for instance, birth rate does not depend on the population size N_n, but rather on the sexually mature individuals. A way to incorporate the delay effect is to consider models like:

$$N_{n+1} = f(N_n, N_{n-R}) , \tag{4.1}$$

where R (an integer) is the delay. We will study the stability of the steady state of these delay models.

4.1.1 Case R = 1

Equation (4.1) becomes:

$$N_{n+1} = f(N_n, N_{n-1}) . \tag{4.2}$$

Set $X_n = \text{col}\{N_{n-1}, N_n\}$. Equation (4.2) can be written:

$$X_{n+1} = F(X_n) , \tag{4.3}$$

with

$$F(X) = \text{col}\{F_x(x, y), F_y(x, y)\} , X = \text{col}\{x, y\},$$

$$F_x(x, y) = y, F_y(x, y) = f(y, x) .$$

A steady point of (3.3) is such that $X_* = \text{col}\{x_*, y_*\}$ and $X_* = F(X_*)$ with $x_* = y_*$ and $x_* = f(x_*, x_*)$. Note that x_* is a steady point of (4.2).

Let us set $\Sigma_n = X_n - X_*$ and linearize (3.3) about X_*:

$$\Sigma_{n+1} = M\Sigma_n + o(\Sigma_n) ,$$

with

$$M = \begin{pmatrix} 0 & 1 \\ \left(\dfrac{\partial f}{\partial y}\right)_{X_*} & \left(\dfrac{\partial f}{\partial x}\right)_{X_*} \end{pmatrix} . \tag{4.4}$$

The eigenvalues of M, given by (4.4), satisfies equation $P(\lambda) = 0$, where:

$$P(\lambda) = \lambda^2 - \lambda\left(\frac{\partial f}{\partial x}\right)_{X_*} - \left(\frac{\partial f}{\partial x}\right)_{X_*}.$$

The steady point X_* is stable if the modulus of the eigenvalues of M are less than 1. In the case of general delay ($R \geq 1$) the approach is the same as for $R = 1$.

4.1.2. Comparison with the system without delay

Let us consider the system without delay associated with the delay model (4.1):

$$N_{n+1} = f(N_n, N_n)\,. \tag{4.5}$$

The steady states of (4.1) and (4.5) are the same. A steady state of the system without delay is stable if:

$$\left|\left(\frac{\partial f}{\partial x}\right)_{X_*} + \left(\frac{\partial f}{\partial y}\right)_{X_*}\right| < 1. \tag{4.6}$$

4.2 Discrete logistic model

The discrete-time logistic model is:

$$\frac{N((n+1)\Delta) - N(n\Delta)}{\Delta} = \rho N(n\Delta)\left(1 - \frac{N(n\Delta)}{\kappa}\right).$$

Let us make the changes of parameters: $r = \rho\Delta + 1$, $K = \kappa(\rho\Delta + 1)/\rho\Delta$ and set $u_n = N(n\Delta)/K$. We then obtain:

$$u_{n+1} = ru_n(1 - u_n)\,. \tag{4.7}$$

This model have been introduced for modeling a population dynamics. From now on, we set:

$$l_r(x) = rx(1 - x)\,. \tag{4.8}$$

We need to work with a positive population size: we will thus assume in the following $0 \leq r \leq 4$ and $0 < u_0 < 1$. We can easily check that the population size remains in the interval $[0, 1]$.

4.2.1 Steady states

The sequence (4.7) has two steady states: 0 and $p = (r - 1)/r$.

- $0 \leq r < 1$. The sequence u_n converges to 0.
- $1 < r < 3$. The state 0 becomes unstable. The state p is stable. We check that the sequence u_n converges to p for any initial condition $0 < u_0 < 1$.
- $3 < r \leq 4$. The steady states 0 and p are both unstable.

We will now study the case $3 < r \leq 4$.

4.2.2 Cycles

Consider the model where the iterative time step is 2:

$$u_{n+2} = l_r(l_r(u_n)) \equiv l_r^2(u_n) .$$

The steady states of the sequence u_{n+2}, apart from 0 and p, $p = (r - 1)/r$, are:

$$u_{\pm} = \frac{r+1 \pm \sqrt{(r+1)(R-3)}}{2r}. \tag{4.9}$$

This shows the existence of a discrete cycle of period 2: if $u_0 = u_+$, then $u_{2n} = u_+$ and $u_{2n+1} = u_-$. This is a first difference between continuous-time and discrete-time models. A one-dimensional continuous-time model has no periodic behavior; a discrete-time model can have a periodic behavior

Definition 4.2.1 *Cycles.*

Consider the iterative sequence $u_{n+1} = f(u_n)$. A cycle of period m is a sequence $c_0, c_1, \dots, c_{m-1}$ such that:

$$c_i = f(c_{i-1}) , \quad f^m(c_0) = c_0 , \quad f^i(c_0) = c_0 \text{ for } i = 1, 2, \dots, m-1 .$$

Proposition 4.2.1 *Stability of a cycle.*

A cycle is stable if $\left|\prod_{i=0}^{m-1} f'(c_i)\right| < 1$.

Indeed, we know that the stability of the sequence $u_{n+m} = f^m(u_n)$ about c_i is given by the condition $|(f^m)'(c_i)| < 1$. But:

$$(f^m)'(c_i) = (f(f(\dots f(c_i))))' = f'(f^{m-1}(c_i))(f^{m-1}(c_i))' = f'(c_{i-1})(f^{m-1}(c_i))' == \prod_{i=0}^{m-1} f'(c_i) .$$

It is possible to check up that the cycle (4.9) of period 2 of the discrete logistic map is stable if $3 < r < 1+\sqrt{6}$ and unstable if $1+\sqrt{6} < r \leq 4$. It is possible to prove the existence of an increasing sequence r_n, with $r_n > 3$ and $\lim r_n = r_c \sim 3,828$, such that the associated discrete logistic map has cycles of period $2n$. To every r_n, a small interval is associated, for which the cycle of period $2n$ is stable. It is possible to prove that the sequence r_n satisfies:

$$\lim_{n\to\infty}\frac{r_n - r_{n-1}}{r_{n+1} - r_n} = \delta \cong 4.6692.....$$

This constant δ is indeed an universal one ([Feigenbaum, M., 1978]). When $r > r_c$, the cycles of period $2n$ become unstable and cycles of period k, $2k$, $4k$, . . ., with k odd, appear. Note that a general result due to Sarkovsky ([Sarkovsky, A., 1964]) ensures that the existence of a cycle of period 3 implies the existence of cycles of period k, with k being an arbitrary integer. The existence of a cycle of period 3 therefore plays a key-role, for the existence of very disturbed behaviors, called chaotic behaviors ([Li T., Yorke J., 1975]).

4.2.3 Chaotic behavior

The mathematical study of this case goes far beyond the scope of this book. In this book, we have no possibilities to give a survey of the general ergodic theory. We will only note that in the case of $r \geq 4$ in the system chaotic behavior are observed. The three following figures enables us to understand the apparition of cycles for the discrete logistic model (for $r = 4$; details see in [Istas J., 2005]).

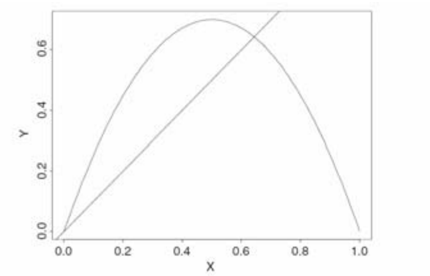


Fig. 4.1. Function $l_r(x)$ for $r = 2.8$

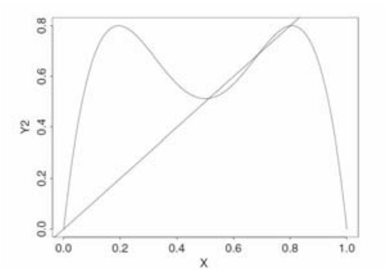
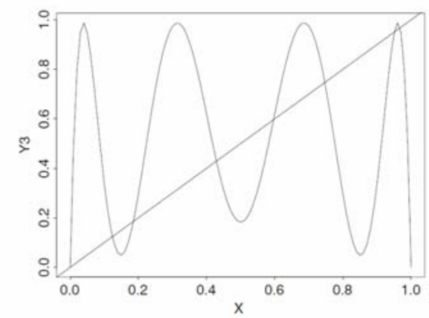


Fig. 4.2. Function $l_r^2(x)$ for $r = 3.2$



Unit 5. Mathematical models of dynamics of two interacting biological populations

5.1. For the first time these mathematical models have been put into consideration in the work of A. Lotka[9] in his research of biochemical reactions (1910 – 1920) and later – of dynamics of biological systems (after 1925). Independently the dynamics of biological systems studied in the works V. Volterra[10] (1926, 1931). In the first period the research of the dynamics of biological systems was concentrated on the mathematical models of population dynamics of two homogeneous biological populations, interacting by the "predator – prey".

Let us first consider in more detail this case of two populations. The best-known model of this type is the classic model of the dynamics of two interacting homogeneous populations – model "predator – prey" (*model of Volterra – Lotka*).

We will give at first a formulation of rather general such model – model, suggested by G.F. Gauze[11]. This model includes the classical model of Volterra – Lotka as rather simple special case.

Dynamics of interaction of two populations coexisting in the same territory – population herbivorous (which representatives are called as the victims or, more precisely, *prey*) and populations of *predators* is considered. We will denote also according to their number $N_1(t)$ and $N_2(t)$ in a time point $t \in \mathbf{R}_{t_0} \equiv [t_0, \infty)$. For lack of predators in this area of the loudspeaker of number of population of the preys it is described by the differential equation of interaction

$$\frac{dN_1(t)}{dt} = M_1[N_1(t)]N_1(t)\,,\ t \in \mathbf{R}_{t_0} \equiv [t_0, \infty), \tag{5.1}$$

where $M_1(N)$ – Malthusian function of herbivorous. It is necessary to add also to the equation (5.1) the following initial condition

$$N_1(t)\big|_{t=t_0+0} = N_1^0 > 0\,. \tag{5.2}$$

If food is available in "unlimited quantity" (that is isn't the limiting factor), then it is possible to consider that Malthusian function of herbivorous has the form $M_1(N) = r_1$, where $r_1 > 0$. In that case "unlimited growth" of the number of population of the preys will be observed.

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[9] Lotka Alfred James (02.03.1880 – 06.12.1949).

[10] Volterra Vito (03.05.1860 – 11.10.1940).

[11] Gause Georgy Franzevich (27.12.1910 - 02.05.1986)

On the contrary, in the absence of the preys the existence of the isolated population of predators is impossible; dynamics of their number in a similar situation is described by the differential equation

$$\frac{dN_2(t)}{dt} = M_2[N_2(t)]N_2(t), \; t \in \mathbf{R}_{t_0} \equiv [t_0, \infty), \tag{5.3}$$

where $M_2(N)$ – Malthusian function of predators, and, obviously, the following condition is satisfied

$$M_2(N) < 0, \quad \forall N \in \mathbf{R}_+ \equiv [0, \infty). \tag{5.4}$$

It is necessary to add also to the equation (5.3) the following initial condition

$$N_2(t)\big|_{t=t_0+0} = N_2^0 > 0. \tag{5.5}$$

In the simplest case, you can assume that $M_2(N) = -r_2$, where $r_2 > 0$ – Malthusian parameter of predators.

Taking into account interaction between the populations leads to a modification of the structure of the equations (5.1), (5.3).

Let $V(N)$ – the number (biomass) of preys consumed an average of one predator per unit of time, if the quantity of population of preys is N. The function $V(N)$ is called *trophic predator function* (*trophic function*) or a *functional response of the predator* (*functional response*). The concept of a functional response was introduced C.S. Holling[12] (1959, 1965) (see, for example, [Swerezhev Yu.M, Logofet D.O., 1978]).

Further, let a certain amount of (say, $k \in (0,1)$) a predator biomass consumption is spent on the reproduction of its population, and the rest is spent on the maintenance of life and hunting activity.

Then the system of differential equations "predator - prey" can be represented as follows:

$$\frac{dN_1(t)}{dt} = M_1[N_1(t)]N_1(t) - V[N_1(t)]N_2(t), \tag{5.6}$$

$$\frac{dN_2(t)}{dt} = \{M_2[N_2(t)] + kV[N_1(t)]\}N_2(t). \tag{5.7}$$

[12] Holling, Crawford Stanley, born 06.12.1930.

It is necessary to add also to the system of equations (5.6), (5.7) the initial conditions (5.2) (5.5) and (5.4) for the Malthusian predators function.

The question of the existence of equilibrium states of the system (5.6) (5.7) (i.e., steady state describing the “coexistence” of population) leads to the consideration of the stationary variant of this system:

$$M_1[N_1^*]N_1^* - V[N_1^*]N_2^* = 0, \tag{5.8}$$

$$\{M_2[N_2^*] + kV[N_1^*]\}N_2^* = 0. \tag{5.9}$$

If the system (5.6), (5.7) has a “positive” equilibrium state – the solution $\{N_1^*, N_2^*\}$ of the system (5.8), (5.9) with the property $N_1^* > 0$, $N_2^* > 0$, then the main interest will be the issue of stability (“sustainability”).

Lets discuss a possible *general form* of the function $V(N)$. It is accepted to mark out some types of trophic functions which forms have some specific and characteristic features only of this type. The quantity of the such classes (types) of trophic functions is usually not really high. According to the tradition which is going back to classical works of Holling C.S. (1959, 1965, 1973), usually there is considered only three (recently – four) such types (see also [Svirezhev Yu.M., Logofet D.O., 1978, S.95], [Svirezhev Yu. M., 1983], [Svirezhev Yu. M., 2008], etc.).

In fig. 2.1 the qualitative type of diagrams of the trophic I-IV functions of types (classification of Holling C.S.) is presented.

<u>*The first type of trophic functions*</u> (or Holling type - I function) is presented by the only function. Its “canonical version" – a piecewise linear function with saturation occurring at values $N \geq N_0$ where $0 < N_0 < \infty$ (see Figure 5.1 (a).).

The fact that trophic function can with sufficient degree of accuracy be considered linear at very small quantities of population of the preys (victims) can be interpreted as follows: the predator is almost always hungry; so, predator doesn't come the saturation and all herbivorous met by him become his food. Thus, fairly following representation of trophic functions I of type:

$$V(N) = \begin{cases} \gamma N, & N \in [0, N_0); \\ V_S, & N \in [N_0, \infty); \end{cases}, \quad V_S \equiv \gamma N_0, \quad \gamma = const > 0, \; N_0 = const > 0. \tag{5.10}$$

However often instead of definition (5.10) the “simplest version” of function $V(N)$ (which is formally “limit” of $V(N)$ when $N_0 \to \infty$) is considered. We will call such option of trophic functions I of type a *functional response of Volterra – Lotka*:

$$V(N) = \gamma N, \quad \gamma = const > 0, \; \forall N \in \mathbf{R}_+. \tag{5.11}$$

So, $V(N)$ from (5.11) is linear for all $N \in \mathbf{R}_+$.

The second type of trophic functions (or Holling type – II function) is presented in fig. 5.1(b). Holling has offered trophic functions of this kind for the description of the “not capable to training” predators (“*silly predator*”). It is considered that trophic II functions are characteristic of invertebrates.

As well as in the case of trophic functions of I type, II function monotone increasing and concave. There is a horizontal asymptote that means that “the effect of saturation” takes place.

Example of trophic function of II type is the functional response of Mikhaelis – Menten – Mono (Michaelis L., Menten M.I., 1913; Monod J., 1942, 1949). The Mikhaelis – Menten – Mono function has the following representation

$$V(N) = \frac{V_S N}{a + N}, \ \forall N \in \mathbf{R}_+. \tag{5.12}$$

Here $a = const > 0$ – “*a semi-saturation constant*” – the number of population with which function $V(N)$ reaches a half size of V_S.

The another of trophic function of II type is the exponential functional response. This functional response describes Poisson process of search of production (cf. [Svirezhev Yu.M., 1987, S.17]) and it can be presented in the following form

$$V(N) = V_S\{1 - e^{-aN}\}, \ \forall N \in \mathbf{R}_+, \ a, c = const > 0. \tag{5.13}$$

The third type of trophic functions (or Holling type – III function) is presented in fig. 5.1(c). This type of trophic functions has been offered by Holling for the description of the vertebrata showing rather difficult behavior, and, for example, “capable to training”. With the same share of convention, as well as above, one may say, that trophic III function is characteristic of “cunning” and “bright” (“*clever predator*”). Typical example – a functional response of “sigmoid” type. This dependence may be represented in the following form

$$V(N) = \frac{V_S N^2}{(a + N)(b + N)}, \ \forall N \in \mathbf{R}_+, \ a, b = const > 0. \tag{5.14}$$

Similar properties are demonstrated by the following function

$$V(N) = \frac{V_S N^n}{a^n + N^n}, \ \forall N \in \mathbf{R}_+, \ a = const > 0, \ n \geq 2. \tag{5.15}$$

<u>The fourth type of trophic functions</u> (or Holling type – IV function) is introduced into consideration in works Taylor R.J. (1984) and Collings J.B. (1997) and includes also nonmonotonic trophic functions.

The functional response like "inhibition" or trophic function of the Mono type – Holdeyna (Monod – Haldane function) [inhibition – suppression, control, braking can be an example of nonmonotonic trophic function (English); a synonym – prohibition]. This dependence may be represented as follows

$$V(N) = \frac{cN}{(a+N)(b+N)}, \ \forall N \in \mathbf{R}_+, \ \ a,b,c = const > 0 . \qquad (5.16)$$

Qualitatively it is presented in fig. 5.1(d).

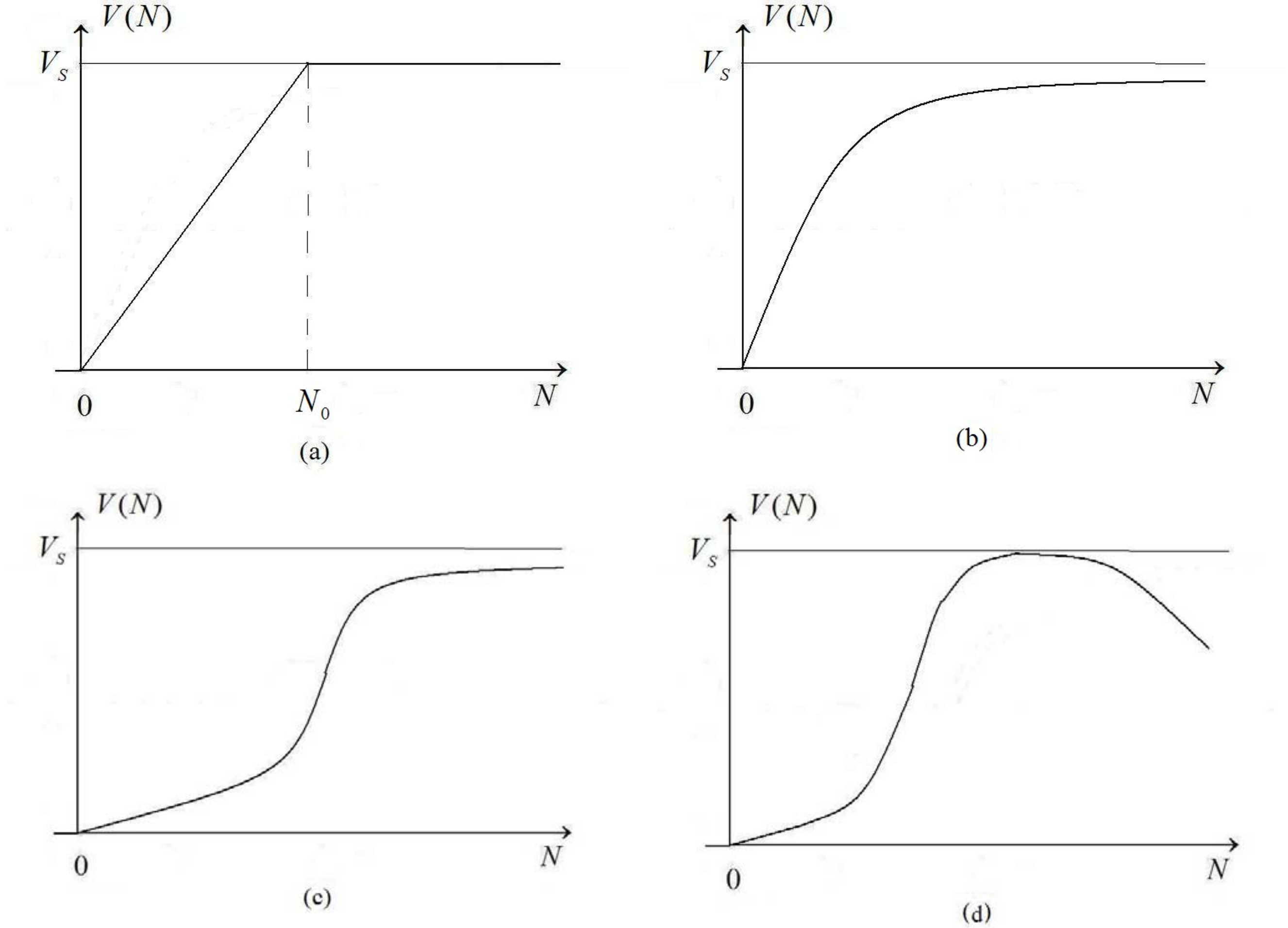


Fig. 5.1. The qualitative form of graphs typical trophic functions

It should be noted that the used above various informal characteristics of predators ("stupid", "not capable of learning", "cunning" or "savvy") should not be misleading. The forms of the trophic functions in fact also determined by the peculiarities of protection of victims of the strategy: if, for example, victims can hide in the shelter, reach the predator, the form of food-predator function is already to a large extent similar to type III.

As noted in the papers of Svirezhev Yu.M. (1983, 2008) one of the most important environmental issues boils down to this question – whether the predator can regulate the population of victims?

Abstracting from the potential ability of a population of victims for self-regulation, it should be recognized that this issue is essentially linked exclusively to the form (kind of) predator trophic function.

At the same time, as stated in Svirezhev Yu.M. (1983, 2008), "stupid" predator as a rule can not "regulate" the quantity of the population of victims – in the sense that the equilibrium state $\{N_1^*, N_2^*\}$ is "globally instable". In the case of "cunning" and "savvy" predator dynamics is much richer: there may be the stability of the steady state, and appearance in its neighborhood of a stable limit cycle.

In that case, if the Malthusian features of preys and predators are the simplest form, so that

$$M_1(N) = r_1 N\,,\ r_1 > 0;\ M_2(N) = -r_2 N\,,\ r_2 > 0\,, \tag{5.17}$$

the system (5.6), (5.7) takes the following form

$$\frac{dN_1(t)}{dt} = r_1 N_1(t) - V[N_1(t)]N_2(t)\,, \tag{5.18}$$

$$\frac{dN_2(t)}{dt} = \{kV[N_1(t)] - r_2\}N_2(t)\,. \tag{5.19}$$

Further specification of the model (2.6), (2.7) can be achieved by selecting a type of explicit form of trophic function of the predator.

If we use the simplest type of functional response – functional response of Volterra – Lotka (5.11), then from (5.18), (5.19) we obtain the following system of ordinary differential equations

$$\frac{dN_1(t)}{dt} = r_1 N_1(t) - \gamma N_1(t)N_2(t) \equiv r_1 N_1(t) - \gamma_1 N_1(t)N_2(t)\,, \tag{5.20}$$

$$\frac{dN_2(t)}{dt} = \{k\gamma N_1(t) - r_2\}N_2(t) \equiv -r_2 N_2(t) + \gamma_2 N_1(t)N_2(t)\,, \tag{5.21}$$

which is the classic *predator – prey model of Volterra – Lotka*.

5.2. We investigate some qualitative properties of the model (5.20), (5.21). First of all, we note that the equation (5.20), (5.21) can also be written in the "more expressive" form.

$$\frac{dN_1(t)}{dt} = \{r_1 - \gamma_1 N_2(t)\} N_1(t), \qquad \frac{dN_2(t)}{dt} = \{\gamma_2 N_1(t) - r_2\} N_2(t). \qquad (5.22)$$

From (5.22) it follows easily that the following relationships are valid (those relationships may be obtained formally by "simple integration"):

$$N_1(t) = N_1(t_0) e^{\int_{t_0}^{t} \{r_1 - \gamma_1 N_2(s)\} ds} \equiv N_1^0 e^{\int_{t_0}^{t} \{r_1 - \gamma_1 N_2(s)\} ds}, \qquad (5.23)$$

$$N_2(t) = N_2(t_0) e^{\int_{t_0}^{t} \{\gamma_2 N_1(s) - r_2\} ds} \equiv N_2^0 e^{\int_{t_0}^{t} \{\gamma_2 N_1(s) - r_2\} ds}, \qquad (5.24)$$

so that, in view of (5.23), (5.24), on the whole interval of existence of solutions of the system (5.20) (5.21) (or, equivalently, (5.22)) the following relations are valid:

$$N_1(t) \geq 0 \Leftrightarrow N_1^0 = N_1(t_0) \geq 0; \quad N_1(t) \leq 0 \Leftrightarrow N_1^0 = N_1(t_0) \leq 0, \qquad (5.25)$$

$$N_2(t) \geq 0 \Leftrightarrow N_2^0 = N_2(t_0) \geq 0; \quad N_2(t) \leq 0 \Leftrightarrow N_2^0 = N_2(t_0) \leq 0. \qquad (5.26)$$

It is clear that the biological sense have only negative initial conditions $(N_1(t_0), N_2(t_0)) \in \mathbf{R}_+ \times \mathbf{R}_+$. In this case, by virtue of (5.25) (5.26) on the whole interval of existence of solutions of (5.20), (5.21) we have the inclusion

$$(N_1(t), N_2(t)) \in \mathbf{R}_+ \times \mathbf{R}_+, \;\; t \in J_{t_0}^T \subseteq \mathbf{R}_{t_0} \equiv [t_0, \infty), \qquad (5.27)$$

where $J_{t_0}^T$ – the maximum interval of the existence of solutions of (5.20), (5.21). Only this situation and further consideration is limited.

First of all, consider the equilibrium state (5.20) – (5.22). It is clear that they are from the following algebraic system of equations

$$\{r_1 - \gamma_1 N_2\} N_1 = 0, \quad \{k\gamma N_1 - r_2\} N_2 = 0, \qquad (5.28)$$

and the system of equations (5.28) has two solutions: trivial solution, and the solution that represents the greatest interest from a biological point of view, a *positive solution*

$$N_1^* = \frac{r_2}{\gamma_2}, \qquad N_2^* = \frac{r_1}{\gamma_1}. \qquad (5.29)$$

The most important feature of the system (5.20) – (5.22) is that it is a *conservative* system. This means that the system (5.20) – (5.22) has a *first integral* $W(N_1, N_2) = const$. We construct this first integral explicitly. It is easy to see that the system (5.20) – (5.22) is possible (in view of (5.29)) written in the form

$$\frac{dN_1(t)}{dt} = \gamma_1 N_1(t)\{N_2^* - N_2(t)\}, \quad \frac{dN_2(t)}{dt} = \gamma_2 N_2(t)\{N_1(t) - N_1^*\}. \tag{5.30}$$

Such representation of system (5.20) – (5.22) is very useful in subsequent constructions. Now consider the system of equations (5.30) in its symmetric form

$$\frac{dN_1}{\gamma_1 N_1 \{N_2^* - N_2\}} = \frac{dN_2}{\gamma_2 N_2 \{N_1 - N_1^*\}}. \tag{5.31}$$

Equation (5.31) can be easily integrated. Indeed, since we have

$$\frac{\gamma_2 \{N_1 - N_1^*\} dN_1}{N_1} = \frac{\gamma_1 \{N_2^* - N_2\} dN_2}{N_2},$$

the relation takes place

$$W(N_1, N_2) \equiv \gamma_2 N_1^* \left[\left(\frac{N_1}{N_1^*} \right) - \ln\left(\frac{N_1}{N_1^*} \right) \right] + \gamma_1 N_2^* \left[\left(\frac{N_2}{N_2^*} \right) - \ln\left(\frac{N_2}{N_2^*} \right) \right] = c, \tag{5.32}$$

where $(N_1, N_2) \in \mathbf{R}_+ \times \mathbf{R}_+$, $c \in \mathbf{R}$ – a constant determined by the initial conditions (5.2), (5.5), so that

$$c = c(N_1^0, N_2^0) \equiv \gamma_2 N_1^* \left[\left(\frac{N_1^0}{N_1^*} \right) - \ln\left(\frac{N_1^0}{N_1^*} \right) \right] + \gamma_1 N_2^* \left[\left(\frac{N_2^0}{N_2^*} \right) - \ln\left(\frac{N_2^0}{N_2^*} \right) \right]. \tag{5.33}$$

Note that (in view of (2.29)) we have the equality

$$c(N_1^*, N_2^*) = \gamma_2 N_1^* + \gamma_1 N_2^* = r_1 + r_2 > 0. \tag{5.34}$$

It is easy to see that the first integral (5.32) can be represented in an equivalent form

$$\ln Y(N_1) - \ln X(N_2) = c = \ln C, \tag{5.35}$$

where $X(N_2) = \left(\frac{N_2}{N_2^*} \right)^{r_1} e^{-\gamma_1 N_2}$, $Y(N_1) = \left(\frac{N_1}{N_1^*} \right)^{-r_2} e^{\gamma_2 N_1}$, $C = e^c > 0$.

Note that in (5.32), (5.35) constants $c \in \mathbf{R}$ and $C \in \mathbf{R}_+$ are defined by the conditions (5.2) and (5.5), such that $W(N_1(t_0), N_2(t_0)) = W(N_1^0, N_2^0) = c(N_1^0, N_2^0) = c$, and $C = e^c > 0$. Representation (5.35) implyies directly another very useful relation:

$$Y(N_1) = CX(N_2). \tag{5.36}$$

Equation (5.36) is very useful for the construction of trajectories of the system (5.20) – (5.22), 5.30). The corresponding graphic procedure was proposed by V. Volterra in his famous book (Volterra V. *Leçons sur la theorie mathématique de la lutte pour la vie*. – Paris: Gauthier – Villars et C[ie] Éditeurs, 1931). It is presented in Fig. 5.2.

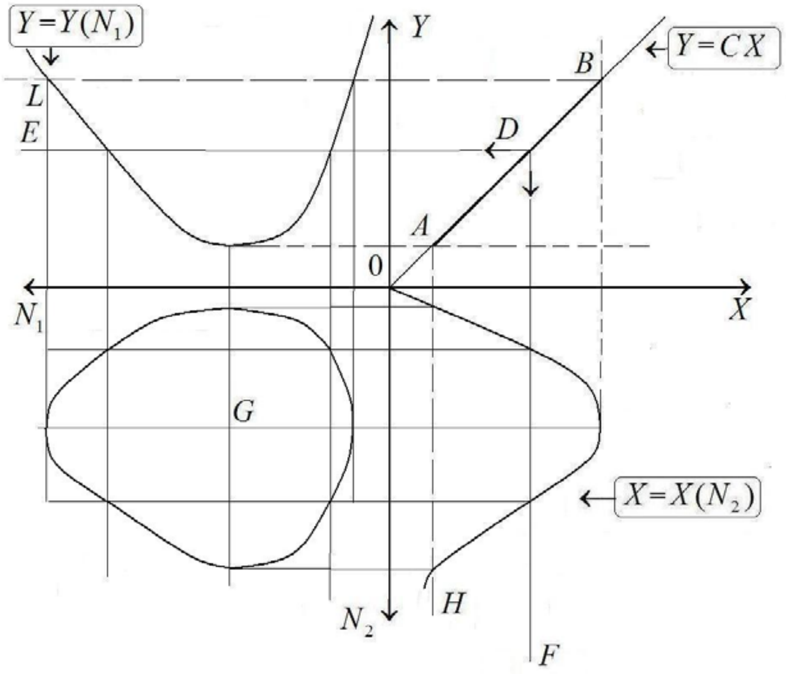


Fig. 5.2. The graphic procedure of V. Volterra

Note that the first integral (5.32) can also be builded immediately directly from a consideration of the system (5.20) – (5.22).

In fact, we multiply (5.20) (or the first of the equations (5.22)) on r_2/N_1, and the equation (5.21) (or the second of the equations (5.22)) – on r_1/N_2, and then sum up the results. We get:

$$\frac{r_2}{N_1}\cdot\frac{dN_1}{dt}+\frac{r_1}{N_2}\cdot\frac{dN_2}{dt}=\frac{r_2}{N_1}\{r_1N_1-\gamma_1N_1N_2\}+\frac{r_1}{N_2}\{-r_2N_2+\gamma_2N_1N_2\}=$$
$$=r_1r_2-\gamma_1r_2N_2-r_1r_2+r_1\gamma_2N_1=r_1\gamma_2N_1-r_2\gamma_1N_2. \qquad (5.37)$$

Further, multiply (5.20) on γ_2, and the equation (5.21) on γ_1, and then sum up the results. We get:

$$\gamma_2\frac{dN_1}{dt}+\gamma_1\frac{dN_2}{dt}=(r_1\gamma_2N_1-\gamma_1\gamma_2N_1N_2)+(-r_2\gamma_1N_2+\gamma_1\gamma_2N_1N_2)=$$

$$= r_1\gamma_2 N_1 - r_2\gamma_1 N_2 . \qquad (5.38)$$

From (5.37) and (5.38) we get:

$$r_2 \frac{d\ln N_1}{dt} + r_1 \frac{d\ln N_2}{dt} = \gamma_2 \frac{dN_1}{dt} + \gamma_1 \frac{dN_2}{dt} . \qquad (5.39)$$

So, from (5.39) we have:

$$\frac{d}{dt}\left\{\ln N_1^{r_2} + \ln N_2^{r_1} - \gamma_2 N_1 - \gamma_1 N_2\right\} = 0 ,$$

and that is (5.32).

As it follows from Fig. 5.2, the trajectory of the system are some kinds of the ovals. If we “turn” the third quadrant of Fig. 5.2, we get a qualitative picture of the trajectories of the system shown in Fig. 5.3

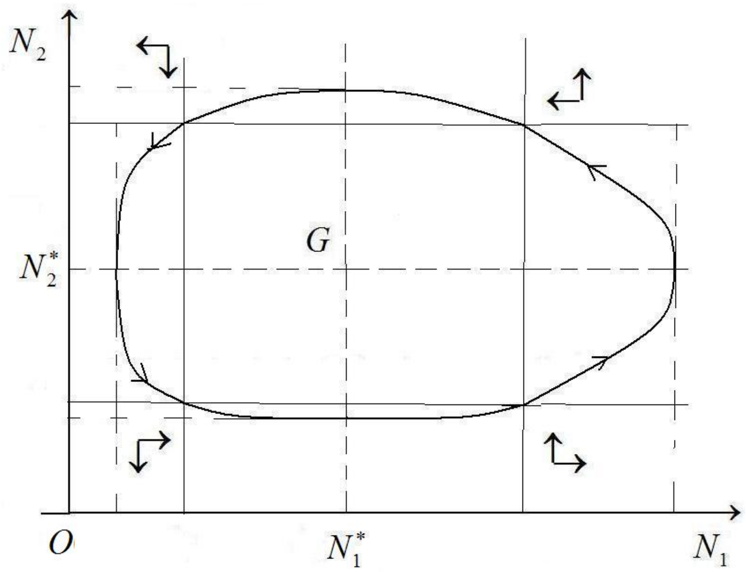


Рис. 5.3. Phase portrait of the system (5.18) – (5.20)

The origin $O(0,0)$ and the point $G(N_1^*, N_2^*)$ are states of equilibrium of (5.20) – (5.22) (5.30). Lets define the type of equilibrium states. Linearization of the system (5.20) – (5.22) in the neighborhood of these points gives us the following result.

The origin $O(0,0)$. The linearized system:

$$\frac{d\xi_1(t)}{dt} = r_1\xi_1(t) , \qquad \frac{d\xi_2(t)}{dt} = -r_2\xi_2(t) . \qquad (5.40)$$

The characteristic equation has the form $(\lambda - r_1)(\lambda + r_2) = 0$, and its roots $\lambda_1 = r_1$ and $\lambda_2 = -r_2$ – the real numbers of opposite signs. Point $O(0,0)$ – is a *saddle point*. The equilibrium state $O(0,0)$ is *unstable*.

Point $G(N_1^*, N_2^*)$. The linearized system has the form

$$\frac{d\xi_1(t)}{dt} = -\frac{r_2\gamma_1}{\gamma_2}\xi_2(t), \qquad \frac{d\xi_2(t)}{dt} = \frac{r_1\gamma_2}{\gamma_1}\xi_1(t). \tag{5.41}$$

The characteristic equation has the form $\lambda^2 + r_1 r_2 = 0$, and its roots $\lambda_{1,2} = \pm i\omega$, $\omega = \sqrt{r_1 r_2}$ – the pure imaginary complex numbers. Point $G(N_1^*, N_2^*)$ – is a singular point of *center*. The equilibrium state $G(N_1^*, N_2^*)$ is stable in the sense of A.M. Lyapunov.

As we know, the center – *structurally unstable equilibrium state*. It is stable, but not asymptotically stable (in the sense of Lyapunov A.M.) equilibrium.

So, within the framework of the classical model of Volterra – Lotka the most interesting equilibrium state is structurally unstable.

Consider very close to the classical model of Volterra – Lotka “generalized model of Volterra – Lotka”, which uses the Malthusian function of herbivorous species of more realistic form – it takes into account the ability of population of preys to self-regulation. Thus, we obtain a system of ordinary differential equations of the form

$$\frac{dN_1(t)}{dt} = r_1 N_1(t)\left[1 - \frac{N_1(t)}{K}\right] - \gamma_1 N_1(t) N_2(t), \tag{5.42}$$

$$\frac{dN_2(t)}{dt} = -r_2 N_2(t) + \gamma_2 N_1(t) N_2(t), \tag{5.43}$$

where K – the capacity of the habitat herbivorous population.

The stationary states of the system (5.42), (5.43) are determined from the relations

$$r_1 N_1\left(1 - \frac{N_1}{K}\right) - \gamma_1 N_1 N_2 = 0, \quad -r_2 N_2 + \gamma_2 N_1 N_2 = 0. \tag{5.44}$$

We shall assume that the natural from a biological point of view the condition $r_2 < \gamma_2 K$ is valid. Then the system of algebraic equations (5.44) has a unique equilibrium state $\{N_1^*, N_2^*\}$, $N_1^* > 0$, $N_2^* > 0$:

$$N_2^* = \frac{r_1}{\gamma_1}\left(1 - \frac{N_1^*}{K}\right), \qquad N_1^* = \frac{r_2}{\gamma_2}. \tag{5.45}$$

Lets denote this equilibrium $G(N_1^*, N_2^*)$. Using (5.45) we get the following system of equations:

$$\frac{dN_1(t)}{dt} = \gamma_1 N_1(t)\left\{\left[N_2^* - N_2(t)\right] + \frac{r_1}{\gamma_1 K}\left[N_1^* - N_1(t)\right]\right\}, \tag{5.46}$$

$$\frac{dN_2(t)}{dt} = \gamma_2 N_2(t)\left\{N_1(t) - N_1^*\right\}. \tag{5.47}$$

Let us introduce the following function of A.M. Lyapunov:

$$U(N_1, N_2) = \gamma_2 N_1^* \Phi\left[\frac{N_1}{N_1^*}\right] + \gamma_1 N_2^* \Phi\left[\frac{N_2}{N_2^*}\right], \tag{5.48}$$

where $\Phi(z) \equiv z - \ln z - 1$, $\forall z \in \mathbf{R}_+$, $\forall (N_1, N_2) \in \mathbf{R}_+ \times \mathbf{R}_+$, and parameters N_1^* and N_2^* are defined in (5.45). Then

$$\frac{dU[N_1(t), N_2(t)]}{dt} = (\gamma_1\gamma_2)\left\{N_1\left(N_2^* - N_2\right)\Phi'\left[\frac{N_1}{N_1^*}\right] + N_2\left(N_1 - N_1^*\right)\Phi'\left[\frac{N_2}{N_2^*}\right] + \right.$$
$$\left. + N_1\left(N_1^* - N_1\right)\frac{r_1}{\gamma_1 K}\Phi'\left[\frac{N_1}{N_1^*}\right]\right\}, \tag{5.49}$$

so

$$\frac{dU[N_1(t), N_2(t)]}{dt} = -\frac{r_1\gamma_2}{K}\left[N_1(t) - N_1^*\right]^2 \le 0. \tag{5.50}$$

Using the theorem of asymptotic stability of E.A. Barbashin – N. N. Krasovsky in this situation we may conclude that the equilibrium state is asymptotically stable in the sense of A.M. Lyapunov. So, “the generalized model” at any values of parameters of system of the ordinary differential equations (5.42), (5.43) can't have periodic movements. At the same time, as it was already noted above, she is more realistic and describes the intraspecific competition arising because of limitation of resources; at the same time trophic function (a functional response) in models are the same.

5.3. The next level complexity presents the following generalization of the classical Volterra – Lotka model – the model of Holling – Tanner – May (Holling C.S., 1965; Tanner J.T., 1966, 1975; May R.M., 1974).

In this model is used the "more realistic" description of interaction of populations. At creation of this model it was supposed that in it existence of periodic movements will be connected not with a special point like center (which is *structurally unstable*), but with existence of limit cycles.

In this model a functional response of Mikhaelis – Menten – Mono is used as trophic function of a predator:

$$V(N_1) = \frac{\gamma_1 N_1}{\alpha + N_1}, \ \gamma_1, \alpha > 0. \qquad (5.51)$$

The mathematical model of Holling – Tanner – May (HTM model) of dynamics of quantity of the biological populations has the following form:

$$\frac{dN_1(t)}{dt} = r_1 N_1(t)\left\{1 - \frac{N_1(t)}{K_1}\right\} - \frac{\gamma_1 N_1(t)}{\alpha + N_1(t)} \cdot N_2(t) \equiv P(N_1 N_2), \qquad (5.52)$$

$$\frac{dN_2(t)}{dt} = r_2 N_2(t)\left\{1 - \frac{N_2(t)}{vN_1(t)}\right\} \equiv Q(N_1 N_2). \qquad (5.53)$$

Here $r_i > 0$ – Malthusian parameters of preys ($i = 1$) and predators ($i = 2$).

The system (5.52), (5.53) may be presented also in the form

$$\frac{dN_1(t)}{dt} = r_1 N_1(t)\left\{\left[1 - \frac{N_1(t)}{K_1}\right] - \frac{\gamma_1 N_2(t)}{\alpha + N_1(t)}\right\}, \ \frac{dN_2(t)}{dt} = r_2 N_2(t)\left\{1 - \frac{N_2(t)}{vN_1(t)}\right\}. \qquad (5.54)$$

The rigorous consideration of the system (5.52), (5.53) (or (5.54)) shows that the phase portrait of this system may be presented as it indicated in the Fig. 5.4.

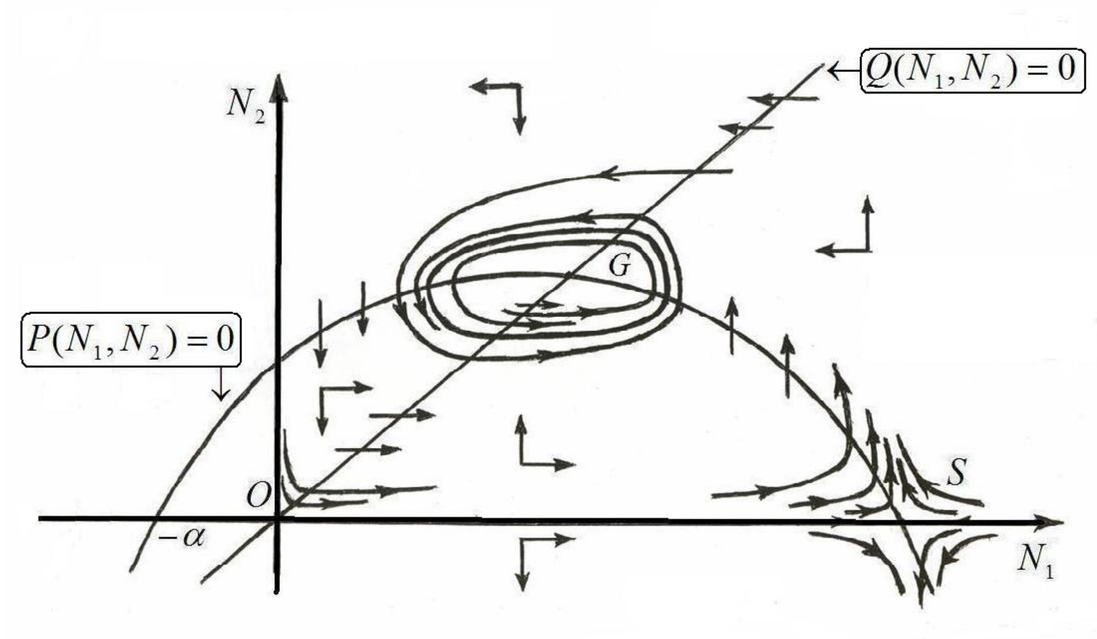


Fig. 5.4. Qualitative picture of trajectories of system (5.52), (5.53), (5.54) in the first quadrant of the plane

The main problem – the problem of existence of the limit cycles in this model – has the positive solution based on the Theorem of Andronov – Hopf (bifurcation of Andronov – Hopf).

Some other models – generalizations of the classical Volterra – Lotka model. Their highly general form may be written as:

$$\frac{dN_1(t)}{dt} = r_1 N_1(t)\left\{1 - \frac{N_1(t)}{K_1}\right\} - V[N_1(t)]N_2(t), \tag{5.55}$$

$$\frac{dN_2(t)}{dt} = r_2 N_2(t)\left\{1 - \frac{N_2(t)}{vN_1(t)}\right\}. \tag{5.56}$$

The partial cases of this general model are *Leslie – Gower model* (Leslie P.H., Gower J.C., 1960)

$$\frac{dN_1(t)}{dt} = r_1 N_1(t)\left\{1 - \frac{N_1(t)}{K_1}\right\} - \gamma_1 N_1(t) N_2(t), \tag{5.57}$$

$$\frac{dN_2(t)}{dt} = r_2 N_2(t)\left\{1 - \frac{N_2(t)}{vN_1(t)}\right\}, \tag{5.58}$$

Rosenzweig – May model (Rosenzweig M., 1971, May R.M., 1972)

$$\frac{dN_1(t)}{dt} = r_1 N_1(t)[1 - \frac{N_1(t)}{K}] - \gamma_1[1 - e^{-c_1 N_1(t)}]N_2(t), \tag{5.59}$$

$$\frac{dN_2(t)}{dt} = \left\{-r_2 + \gamma_2[1 - e^{-c_2 N_1(t)}]\right\}N_2(t),\ 0 < r_2 < \gamma_2 \tag{5.60}$$

and so on.

Even more general view is presented in two widely known works of A.N. Kolmogorov (Kolmogoroff A.N., 1936; Kolmogorov A.N., 1972).

Kolmogorov's model of dynamics of two interacting populations is the following system of the differential equations:

$$\frac{dN_1(t)}{dt} = K_1[N_1(t), N_2(t)]N_1(t), \tag{5.61}$$

$$\frac{dN_2(t)}{dt} = K_2[N_1(t), N_2(t)]N_2(t). \tag{5.62}$$

Theorem (Kolmogorov A.N., 1936, 1972).

Let functions $K_1(N_1, N_2)$, $K_2(N_1, N_2)$, $(N_1, N_2) \in \mathbf{R}_+ \times \mathbf{R}_+$, are continuous with the first partial derivatives. Let, further, inequalities would hold

- $\frac{\partial K_1(N_1, N_2)}{\partial N_2} < 0$; $\quad \frac{\partial K_2(N_1, N_2)}{\partial N_2} < 0$; $\quad K_1(0,0) > 0$;
- $N_1 \frac{\partial K_1(N_1, N_2)}{\partial N_1} + N_2 \frac{\partial K_1(N_1, N_2)}{\partial N_2} < 0$; $N_1 \frac{\partial K_2(N_1, N_2)}{\partial N_1} + N_2 \frac{\partial K_2(N_1, N_2)}{\partial N_2} > 0$,

and, besides, there are real numbers $A, B, C \in (0, \infty)$, $B > C$, such that equalities $K_1(0, A) = 0$; $K_1(B,0) = 0$; $K_2(C,0) = 0$ take place.

Then the model (5.61), (5.62) has in the first quadrant equilibrium state and either it is asymptotically stable equilibrium state, or, in opposite case, in its vicinity there exist a stable limit cycle.

Some problems for self study

Problem 1. Try to study the solution of the following *Leslie – Gower model* (Leslie P.H., Gower J.C., 1960)

$$\frac{dN_1(t)}{dt} = r_1 N_1(t)\left\{1 - \frac{N_1(t)}{K_1}\right\} - \gamma_1 N_1(t) N_2(t), \tag{5.57}$$

$$\frac{dN_2(t)}{dt} = r_2 N_2(t)\left\{1 - \frac{N_2(t)}{v N_1(t)}\right\}, \tag{5.58}$$

Problem 2. Try to study the solution of the following *Rosenzweig – May model* (Rosenzweig M., 1971, May R.M., 1972)

$$\frac{dN_1(t)}{dt} = r_1 N_1(t)[1 - \frac{N_1(t)}{K}] - \gamma_1 [1 - e^{-c_1 N_1(t)}] N_2(t), \tag{5.59}$$

$$\frac{dN_2(t)}{dt} = \left\{ -r_2 + \gamma_2 [1 - e^{-c_2 N_1(t)}] \right\} N_2(t),\ 0 < r_2 < \gamma_2 \tag{5.60}$$

Unit 6. Some Mathematical models of Neuroscience

6.1. Some historical and terminological comments

This unit is devoted to description of some basic elements of Neuroscience. Neuroscience is currently one of the most fast growing scientific fields. This is largely due to recent advances in experimental techniques and associated methods for analysis of “big data”. The main aim of this part – to show how mathematical models and their analyses are contributing to understanding of some biological problems connected with studies of brain and central nervous system. This section is largely based on the materials of a review article [Holmes P., 2014].

Mathematical treatments of the nervous system began in the mid 20th century. An early example is Norbert Wiener’s “Cybernetics,” published in 1948 and based on work with the Mexican physiologist Arturo Rosenblueth. He also discussed the relationship between digital computers (then in their infancy) and neural circuits, a theme that John von Neumann subsequently addressed in a book “The Computer and the Brain” (1958). In developing cybernetics, Wiener drew on von Neumann’s earlier works in analysis, ergodic theory, computation and game theory, as well his own studies of Brownian motion (so called *Wiener processes*).

Books of Wiener and von Neumann were directed at the brain and nervous system *in toto*. The first cellular-level mathematical model of a single neuron was developed in the early 1950s by the British physiologists Hodgkin and Huxley. This work, which won them the Nobel Prize in Physiology in 1963, grew out of a long series of experiments on the giant axon of the squid (*Loligo*).

Now their pioneering work on mathematical neuroscience has grown into the new scientific discipline. Description of this science may be found in set the lecture courses, textbooks, review articles, books etc. “The number of mathematical models must now exceed the catalogue of brain areas by several orders of magnitude” [Holmes P., 2014; P. 203].

These models can be of two broad types: empirical (also called descriptive or phenomenological), or mechanistic. The former ignore (possibly unknown) anatomical structure and physiology, and seek to reproduce input–output or stimulus–response relationships of the system under study.

Mechanistic models attempt to describe structure and function in some detail, reproducing observed behaviors by appropriate choice of model components and parameters and thereby revealing mechanisms responsible for those behaviors.

Models can reside throughout a continuum from molecular to organismal scales, and many are not easily classifiable, but one common feature is *nonlinearity*. Unlike much of physical science and engineering, biology is inherently nonlinear.

For example, the functions describing ion channels opening in cells in response to transmembrane voltage increase or characterizing neural firing rate dependence on input current are typically bounded above and below, and often modeled by “sigmoids” (a sigmoid function is a mathematical function having an “S” shape (sigmoid curve). Often, sigmoid function refers to the special case of the logistic function[13].).

The basic components of the nervous system are neurons = electrically active cells that can generate and propagate signals over distance. These signals are action potentials (APs, or spikes)[14].

Structurally, neurons come in many shapes and sizes, but all share the basic features of a *soma* or cell body, *dendrites*: multiply branching extensions that receive signals from other neurons, and an *axon*, a cable-like extension that may also be branched, along which APs propagate to other neurons[15]. The connections between axons and dendrites are called *synapses*, and they may be electrical, communicating voltage differences, or chemical, releasing neurotransmitters upon the arrival of an AP from the presynaptic cell. Functionally, neurons are either *excitatory* or *inhibitory*, tending to increase or depress the transmembrane voltage of postsynaptic cells to which they connect.

6.2. The Components: Neurons, Synapses and the Hodgkin–Huxley Equations

As noted above, following years of beautiful and painstaking experiments reported in an impressive series of papers (in the period 1949 - 1952), Hodgkin and Huxley created the first mathematical model for the AP. This work gained them a Nobel prize in 1963, along with J.C. Eccles.

They used the giant axon of a squid. The cell's size allowed them to thread a silver wire through it, equalizing voltages along the axon, thus removing spatial variations and allowing them to describe its dynamics in terms of nonlinear ordinary differential equations (ODEs):

$$\begin{aligned} C_m \frac{\mathrm{d}v}{\mathrm{d}t} &= -\bar{g}_{\mathrm{K}} n^4 (v - v_{\mathrm{K}}) - \bar{g}_{\mathrm{Na}} m^3 h (v - v_{\mathrm{Na}}) - \bar{g}_{\mathrm{L}} (v - v_{\mathrm{L}}) + I, \\ \frac{\mathrm{d}m}{\mathrm{d}t} &= \alpha_m(v)(1 - m) - \beta_m(v) m, \\ \frac{\mathrm{d}n}{\mathrm{d}t} &= \alpha_n(v)(1 - n) - \beta_n(v) n, \\ \frac{\mathrm{d}h}{\mathrm{d}t} &= \alpha_h(v)(1 - h) - \beta_h(v) h. \end{aligned} \tag{6.1}$$

[13] https://en.wikipedia.org/wiki/Sigmoid_function

[14] Abbreviations: HH = Hodgkin–Huxley equations for the generation and propagation of a single action potential; AP, or spike = action potential; DD process = drift-diffusion process; SPRT = sequential probability ratio test.

[15] Biologists refer to dendrites and axons as *processes*: confusing terminology for a mathematician!

The figure 6.1. shows an equivalent circuit diagram for the giant axon of the squid. She was the basis for the mathematical description of the giant axon of the squid. The result of the constructions of Hodgkin and Huxley is the following system of ODE (6.1).

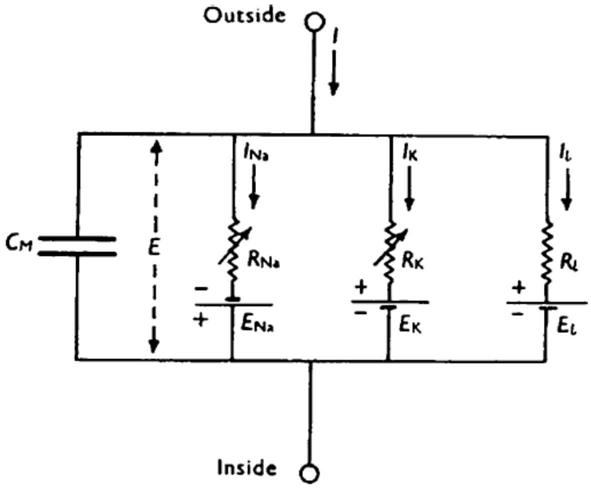


Fig. 6.1. Equivalent circuit for the giant axon of squid

The coefficients of this system are quite complicated:

$$\alpha_m(v) = 0.1\frac{25-v}{\exp(\frac{25-v}{10})-1}, \qquad \beta_m(v) = 4\exp\left(\frac{-v}{18}\right),$$
$$\alpha_h(v) = 0.07\exp\left(\frac{-v}{20}\right), \qquad \beta_h(v) = \frac{1}{\exp(\frac{30-v}{10})+1}, \tag{6.2}$$
$$\alpha_n(v) = 0.01\frac{10-v}{\exp(\frac{10-v}{10})-1}, \qquad \beta_n(v) = 0.125\exp\left(\frac{-v}{80}\right),$$

To emphasize the equilibrium potential $n_\infty(v)$ at which n remains constant, and the time scale $\tau_n(v)$, the gating equations may be rewritten as follows:

$$\frac{dn}{dt} = \frac{n_\infty(v)-n}{\tau_n(v)}, \quad \text{where}$$
$$n_\infty(v) = \frac{\alpha_n(v)}{\alpha_n(v)+\beta_n(v)}, \; \tau_n(v) = \frac{1}{\alpha_n(v)+\beta_n(v)} \tag{6.3}$$

with analogous expressions for m and h.

6.3 Two-Dimensional Reductions of HH

There are two ways to simplify Hodgkin-Huxley equations. Those are:

- approach of Krinsky – Kokoz (1973) and, independently, Rinzel (1985);

➢ approach of FitzHugh – Nagumo (FN).

In the first approach, we obtain the following system differential equations:

$$C_m \frac{dv}{dt} = -\bar{g}_K n^4 (v - v_K) - \bar{g}_{Na} m_\infty(v)^3 (a - n)(v - v_{Na}) - \bar{g}_L (v - v_L) + I,$$

$$\tau_n(v) \frac{dn}{dt} = n_\infty(v) - v.$$

This reduction to a planar system can be made rigorous by use of geometric singular perturbation methods.

The study of this model (in the first approach) leads to interesting conclusions. It is, in particular, about the existence (for certain values of the parameters) stable limit cycle (see. Fig. 6.2).

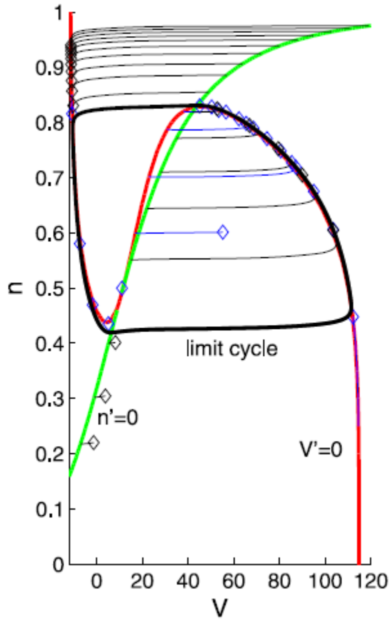


Fig. 6.2. Phase planes of the reduced HH equations

In the second approach, we obtain the following system differential equations:

$$\dot{v} = \frac{1}{\tau_v}\left(v - \frac{v^3}{3} - r + I\right),$$

$$\dot{r} = \frac{1}{\tau_r}(-r + 1.25v + 1.5),$$

Timescales are normally chosen so that $\tau_v \ll \tau_r = O(1)$ to preserve the relaxation oscillation with fast rise and fall in v.

The study of FizHugh – Nagumo model also leads to interesting conclusions. Phase portrait on the plane of the FizHugh–Nagumo system of equations is presented at Fig. 6.3.

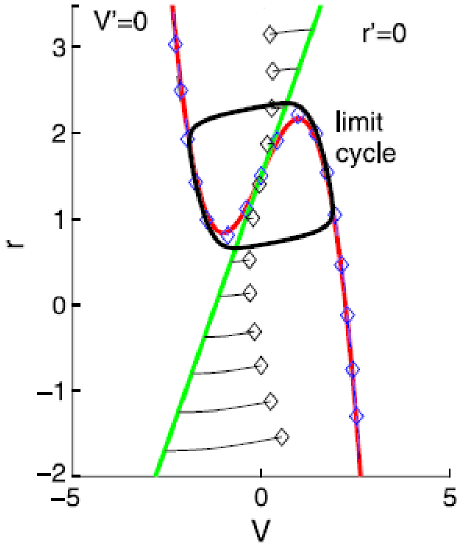


Fig. 6.3. Phase portrait of the FizHugh – Nagumo system

Currently, we have achieved significant success in the construction and study of mathematical models. Of course, much remains unexplored problems. In the [Holmes P., 2014] listed some problems that now seem most relevant. These include:

- Further development of the theory and analytical methods for hybrid dynamical systems, especially for (large) networks of integrate-and-fire cells.
- Better descriptions of, and methods for extracting macroscopic activity states in averaging over large cell populations.
- Nested sets of models for simple tasks, fitted to electrophysiological and behavioral data.
- Further use of time scale separation in creating and analyzing models of cognitive dynamics.
- Analyses of iterative learning algorithms as dynamical systems.

Some problems for self study

Problem 1. In some cases pulses (spikes) propagation may be described by the Fitzhugh – Nagumo type system of equations

$$\varepsilon\frac{dx(t)}{dt}=x\left(1-x^2\right)-y,\quad \frac{dy(t)}{dt}=x-\xi,$$

where $\varepsilon>0$ is a (*small*) parameter and $\xi\in\mathbf{R}$ is a critical parameter (to be chosen). Try to investigate this mathematical model (remark: it is the singularly perturbed system of ordinary differential equations).

Appendix

In this chapter we review some facts of the basic mathematical theories which are frequently used in the real researches. We have included some of the qualitative theory of ordinary Differential Equations and Calculus of One and Several Variables, needed elsewhere in the theory of ordinary Differential Equations. The material, described in the present appendix, is based on corresponding sections of some known monographies and university textbooks. The listed below books may be used for a deeper studying of the corresponding subject: [Elaydi S.N., 2005], [Guckenheimer J., Holmes P., 1990], [Hirst K.E., 2006], [Istas J., 2005], [Kuznetsov Y.A., 1998], [Shilnikov L.P., 2003], [Wiggins S., 1990].

A.1 Ordinary differential equations

Let I be an interval of the form $[t_0, T]$, $[t_0, T)$ or $[t_0,+\infty)$. Let f be a continuous function from $\mathbf{R}^m$ into $\mathbf{R}^m$ and let $y_0 \in \mathbf{R}^m$. We are looking for a continuous differentiable function y, defined from I into $\mathbf{R}^m$, such that, for every $t \in I$:

$$y'(t) = f(y(t)) \,, \; y(t_0) = y_0 \,. \tag{A.1}$$

The equation (A.1) is a first order differential equation. Let us recall that a p-order equation like

$$z^{(p)}(t) = \varphi(z(t), z'(t), \ldots, z^{(p-1)}(t)) \,,$$

is amenable into a first order equation like (A.1) by the transformation $y_1(t) = z(t)$, $y_2(t) = z'(t), \ldots, y_p(t) = z^{(p-1)}(t)$.

Theorem A.1.1 *Cauchy-Lipschitz. If the function f satisfies the Lipschitz condition:*

$$|f(y) - f(z)| \leq L|y - z| \,,$$

for all $(y, z) \in \mathbf{R}^{2m}$*, then the problem* (A.1) *has a unique solution.*

Definition A.1.1 *Trajectory. A trajectory is the set $\{y(t),\, t \in I\}$, where y is a solution of (A.1).*

Definition A.1.2 *Stability. Let* $I = [t_0,+\infty[$*. A solution ψ of* (A.1) *is called a stable solution if, for all* $\varepsilon > 0$*, there exists* $\delta > 0$ *such that, for any solution φ of* (A.1) *satisfying:*

$$|\varphi(t_0) - \psi(t_0)| \leq \delta \,,$$

we have, for all $t \geq t_0$,

$$|\varphi(t) - \psi(t)| \leq \varepsilon \,.$$

Moreover if we have $\lim_{t\to+\infty}|\varphi(t) - \psi(t)| = 0$, *then we say that the solution* ψ *is asymptotically stable.*

We are interested in the steady states, defined by:

$$f(y^*) = 0 .$$

The problem (A.1) with initial condition $y(t_0) = y^*$ admits the solution $y(t) \equiv y^*$. Therefore, we will speak, with a minor abuse of language, of the stability of y^*. The following results concern the stability of the solution near a steady state y^*. Without loss of generality, we will assume that $y^* = 0$.

A.1.1 Stability when *m* = 1

Assume that (A.1) takes the form:

$$y'(t) = ay(t) + g(y(t)) ,$$

where $g(y) = O(|y|1+\varepsilon)$, $\varepsilon > 0$, as $y \to 0$. Then:
1. $a > 0$. 0 is unstable.
2. $a < 0$. 0 is asymptotically stable.

A.1.2 Global behavior when *m* = 1

Let us consider the ordinary differential equation:

$$y'(t) = f(y(t)) ,$$

with initial condition $y(t_0) = y_0$. The qualitative study of the trajectory is done the following way.

1. Assume $f(y_0) < 0$. Denote, when it exists, $y\_ = \sup\{y \le y0, f(y) = 0\}$. The trajectory coming from $y0$ cannot come back to $y0$; this is forbidden by the Cauchy – Lipschitz Theorem that ensures the uniqueness of the solution. For the same reason, the trajectory is not allowed to cross the point $y\_$. The trajectory remains into the interval $[y\_, y0]$. On this interval $[y\_, y0]$, the function f is negative. The derivative of the function y is therefore negative. Function y is decreasing and bounded. Function y converges to a limit as $t \to +\infty$. This limit has to be a steady point. If $y\_$ does not exist, we show that the trajectory converges to $-\infty$ as $t \to +\infty$ with the same arguments.

2. Assume $f(y_0) > 0$. The same arguments prove that the trajectory converges, as $t \to +\infty$, to the smallest zero of function f that is greater than $y0$, when it exists. Else, the trajectory converges as $t \to +\infty$ t_0 $+\infty$. 3. Assume $f(y_0) = 0$. This is a steady point and the trajectory remains on this point.

Especially, an oscillating or asymptotically oscillating behavior is not possible in one dimension.

A.1.3 Stability when *m* = 2

Local behavior of a linear system.

Consider the linear system:

$$y'_1 = ay_1 + by_2 \ , \ y'_2 = cy_1 + dy_2 \ . \tag{A.2}$$

Let A be the matrix

$$A = \begin{pmatrix} a & b \\ c & d \end{pmatrix}.$$

This matrix is sometimes called the stability matrix. Assume $\det(A) = 0$. Let λ, μ the eigenvalues of A. These eigenvalues can be real or complex numbers. If $\lambda = \alpha + i\beta$ (α, β real numbers, $\beta = 0$) is a complex number, then $\mu = \alpha - i\beta$ is the other eigenvalue. There exists a real non-singular matrix T such that $J = TAT^{-1}$ has one of the following forms:

$$J = \begin{pmatrix} \lambda & 0 \\ 0 & \lambda \end{pmatrix} \quad \lambda \neq 0 \tag{A.3}$$

$$J = \begin{pmatrix} \lambda & 0 \\ 0 & \mu \end{pmatrix} \quad \mu < \lambda < 0 \text{ or } 0 < \mu < \lambda \tag{A.4}$$

$$J = \begin{pmatrix} \lambda & 0 \\ \gamma & \lambda \end{pmatrix} \quad \lambda \neq 0, \ \gamma > 0 \tag{A.5}$$

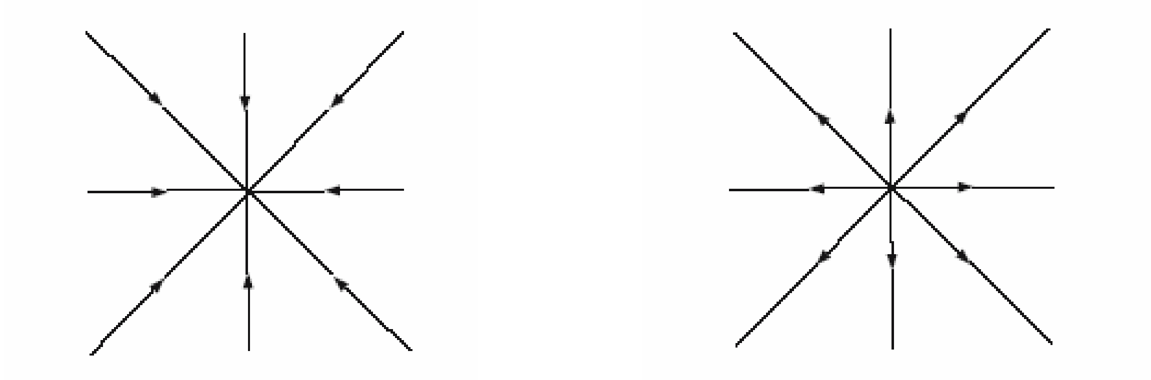
$$J = \begin{pmatrix} \lambda & 0 \\ 0 & \mu \end{pmatrix} \quad \lambda < 0 < \mu \tag{A.6}$$

$$J = \begin{pmatrix} \alpha & \beta \\ -\beta & \alpha \end{pmatrix} \quad \alpha \neq 0, \ \beta \neq 0 \tag{A.7}$$

$$J = \begin{pmatrix} 0 & \beta \\ -\beta & 0 \end{pmatrix} \quad \beta \neq 0 \ . \tag{A.8}$$

The local behavior near (0, 0) and the usual terminology are given by the following figures.

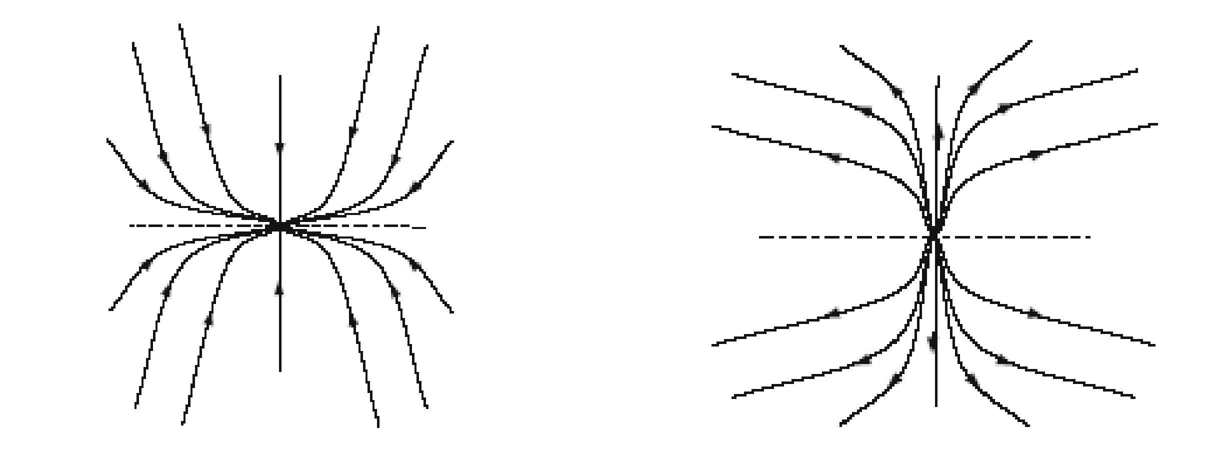
1. Case A.3 a) $\lambda < 0$; b) $\lambda > 0$.



(a) Stable proper node (b) Unstable proper node

Fig. A.1. Stable and Unstable proper nodes

2. Case A.4 a) $\mu < \lambda < 0$; b) $0 < \mu < \lambda$.



(a) Stable node (b) Unstable node

Fig. A.2. Stable and Unstable nodes

3. Case A.5 a) $\lambda < 0$; b) $\lambda > 0$.

(a) Stable improper node (b) Unstable improper node

Fig. A.3. Stable and Unstable improper nodes

4. Case A.6.

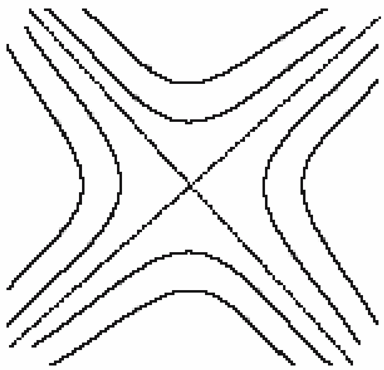
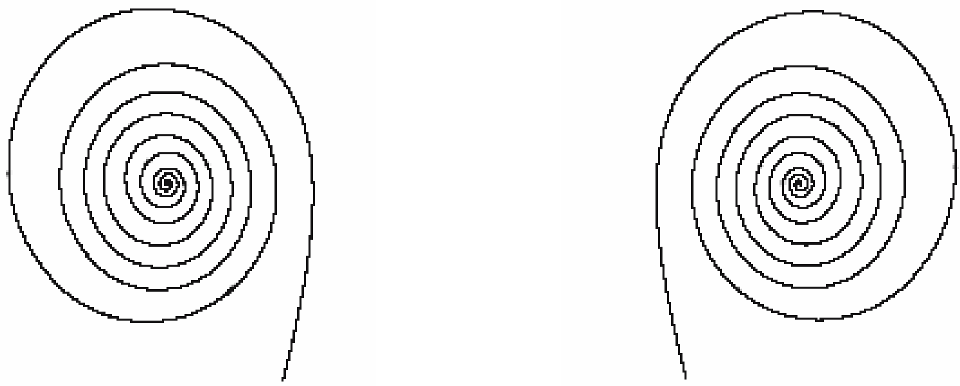


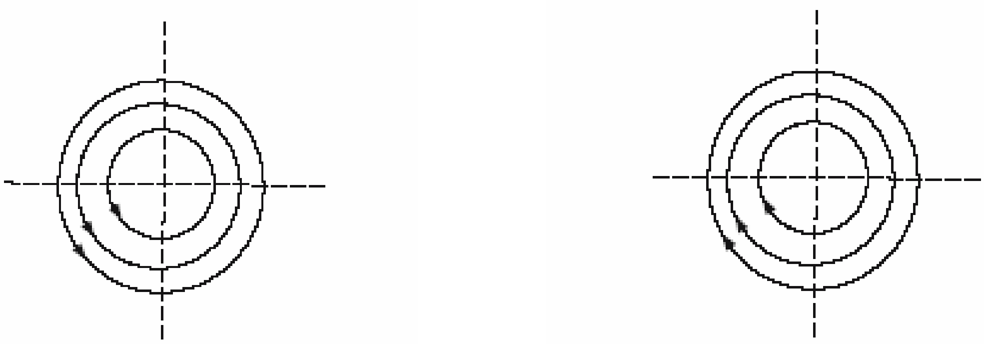
Fig. A.4. Saddle point

5. Case A.7 a) $\alpha < 0, \beta < 0$; b) $\alpha > 0, \beta < 0$.
6. Case A.8 a) $\beta < 0$; b) $\beta > 0$.



(a) Stable focus (b) Unstable focus

Fig. A.5. Stable and Unstable focus ("spiral")



(a) (b)

Fig. A.6. Centre (elliptic fixed point)

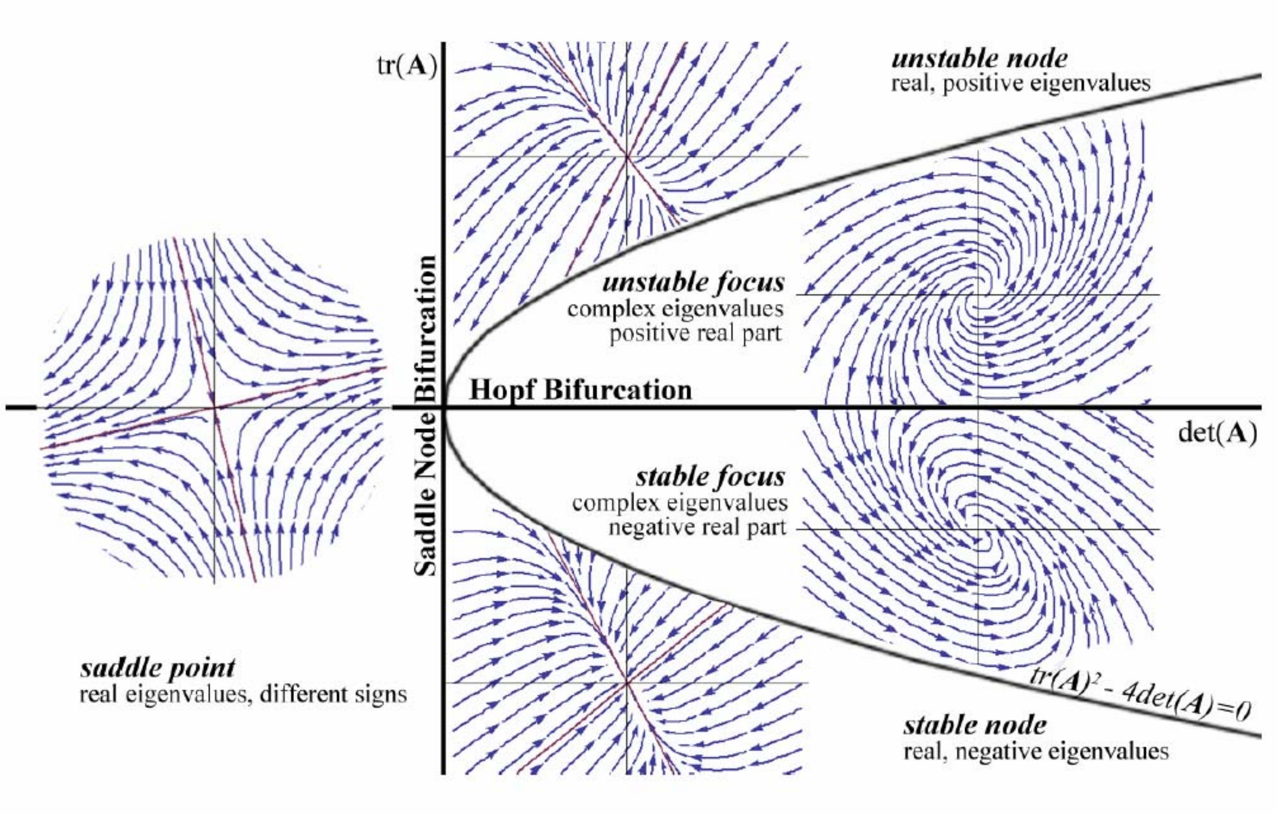


Fig. A.7. Classification of equilibria and their associated eigenvalues

Local behavior of a non-linear system

Consider the non-linear system:

$$y'_1 = ay_1 + by_2 + g_1(y_1, y_2)\,,\;\; y'_2 = cy_1 + dy_2 + g_2(y_1, y_2)\,. \qquad \text{(A.9)}$$

Set $r = \sqrt{y_1^2 + y_2^2}$. Assume the existence of $\varepsilon > 0$ such that, near (0, 0), we have $g_1(y_1, y_2) = O(r^{1+\varepsilon})$, $g_2(y_1, y_2) = O(r^{1+\varepsilon})$ and such that $\partial g_1/\partial_{y2}$ and $\partial g_2/\partial y_1$ exist and are continuous on a neighborhood of (0, 0).

The local behavior of the non-linear system (A.9) can be deduced from the local behavior of the associated linear system (A.2).

1. A node for A.2 remains a node for A.9 and keeps the same stability.
2. A proper node for A.2 remains a proper node for A.9 and keeps the same stability.
3. An elliptic fixed point for A.2 becomes an elliptic fixed point or a node (stable or unstable) for A.9.
4. If A.2 is an unstable improper node, then every trajectory of A.9 converges (or keeps away from) to the origin with an angle of 0, $\pi/2$, π or $3\pi/2$ with the axis of x; the stability is kept.
5. If A.2 is a saddle point, then there exists a trajectory converging to the origin with an angle of 0, one converging to the origin with angle of π, the other keeping away from the origin.

A.1.4 Global behavior when *m* = 2

So far, we only considered the local behavior of the differential equations near the steady state. These behaviors have been given when $m = 2$, but can be easily generalized when $m > 2$. We will now give some global properties. We must keep in mind that these global properties are not available when $m > 2$ anymore.

Consider the following system:

$$y'_1 = f_1(y_1, y_2)\ ,\ \ y'_2 = f_2(y_1, y_2)\ .$$

Assume that $f = \mathrm{Col}(f_1, f_2)$ is defined and continuous on an open bounded domain D of $\mathbf{R}^2$. Recall that a point y^* such that $f(y^*) = 0$ is called a steady state and that a point such that $f(y^*) = 0$ is called a regular point.

Definition A.1.3 *Limit point.*

A point Q is a limit point of the trajectory C if there exists a sequence t_n, with $\lim_{n\to+\infty} t_n = +\infty$, *such that* $(y_1(t_n), y_2(t_n))$ *converges to Q as* $n \to +\infty$. *The set of limit points Q of C is denoted by* $L(C)$.

Theorem A.1.2 *Poincare-Bendixson.*

Assume C to be contained in a closed subset $K \subset D$. If $L(C)$ only contains regular points, then

1. either $C = L(C)$ and C is a periodic trajectory;

2. either $L(C)$ is a periodic trajectory. We say then that C is a limit cycle.

Theorem A.1.3 *Classification of limit trajectories.*

Assume C being contained in a closed subset $K \subset D$. Assume that D only contains a finite number of steady states, then:

1. either $L(C)$ is reduced to a unique steady point, and C converges to this steady point as $t \to +\infty$;

2. either $L(C)$ is a periodic trajectory;

3. either $L(C)$ contains a finite number of steady states and a set of trajectories, each of them converging to a steady state as $t \to +\infty$.

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Учебно-методическое пособие

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