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“Ukrainian Medical Stomatological Academy”

“APPROVED”
at the meeting of the Department
of Medical Informatics, Medical Biophysics
«27» august 2020
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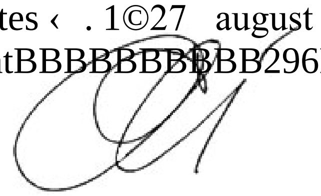
Head of departmentBBBBBBBBBB296LONRYD



METHODICAL GUIDANCE

IRUVWXGHQWVHOI-directed work when preparing and during the practical session

Academic Subject	Medical Information Science
Module No 2	Medical knowledge and decision making in medicine and dentistry
Topic	Modeling in biology and medicine
Year of study	2
6SHFLDOLW\	Foreign Student Training (0HGFLQH6WRPDWRORJ\)
Number of academic hours	2

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1. **Relevance of the topic**:

The topic is very important for future doctors in their professional activity, positively influences the students in their attitude to the future profession, forms professional skills and experience as well as taking as a principle the knowledge of the subject learned.

Studying the complex processes which appear in the nature, in a human body or at carrying out of research experiments, we not always can take into account all existing factors: from them more powerful and the some people it is possible to ignore some. Thus models of such processes, the phenomena are developed, which capable to substitute for them completely and at which studying we can receive the new information on them.

2. **The specific aims**:

To have general knowledge of the topic studied
To understand, to remember and to use the knowledge received
To form the professional experience by reviewing, training and authorizing it
To be able to carry out laboratory and experimental work
To know definition of concept of model, their types;
To know the basic stages of mathematical model operation;
To be able to create mathematical models, to explore them.

3. **Basic knowledge and skills necessary to study the topic (inter-disciplinary integration).**

Previous (providing disciplines)	**Obtainable skills**
Informatics bases	- To create algorithm of medical tasks; To set sequence of actions to form knowledge for use in decision-support system;
The social medicine	To know the basic directions of mathematical models for forecasting diseases; To apply the solution of mathematical models to forecasting diseases. To find out advantage and disadvantages of each kind of model. To find out how it is possible to prognosticate events with the help of mathematical models.

4. **The tasks for students' individual work**

4.1.The list of basic term, parameters, characteristics, which student should master while preparin for the class.

Term	Definition
Model	Model is an artificial object with some nature which substitute or reflect investigated object such as investigators can obtain new information about original object during studying of model
Mathematical model	It is system of mathematical functions, equations, and formulas, which describe some characteristics of process or appearance.
Cybernetic model	It is electronic device or computer programs, which imitate information processes in live organism.
Probabilistic model	Such models based on statistically grounded approximation of empiric distribution.
Deterministic model	Deterministic model is one in which every set of variable states is uniquely determined by parameters in the model and by sets of previous

	states of these variables.
Probabilistic model	In a stochastic model, randomness is present, and variable states are not described by unique values, but rather by probability distributions.

4.2 Theoretical questions for the class (to the topic):

1. To define as model. Classification of models used in medicine and biology.
2. To number stages of model operation.
3. To tell about mathematical model “predators - victims”.
5. To tell about mathematical model operation in an immunology.
6. To tell about mathematical model grows of a population of bacteria.
7. To tell about mathematical model operation of diffusion spreading f a contagion in settlement.

4.3 Practical tasks pertaining to the topic and to be completed during the class:

Test

1) What is “the model”?

a) artificially created by man object arbitrary nature that replaces or reproduces the object in question;

b) a new object that reflects the properties of the object, which are important for the research;

c) a description of the object which is studied;

d) a new object that reflects all properties of the original object;

e) a description of the object with graphs and functions.

2) Which of the variants can be considered as a biological model?

a) a description of the original object using mathematical formulas;

b) another alive object that reflects the essential characteristics and properties of the original object;

c) the collection of data in a table containing information about qualitative and quantitative characteristics of the original object;

d) a description of the object with the original natural language;

e) a description of the original object with a formal language.

3) What time people started to use mathematical modeling as a method of scientific knowledge?

a) since the first human;

b) when were used the laboratory animals first time;

c) when laid the foundations of differential and integral calculus;

d) since the creation of the universe;

e) recently, in the 21st century.

4) What is the mathematical model?

a) description of the scheme;

b) a set of data containing information about the quantitative characteristics of the object and its behavior;

c) many simbols;

d) a set of mathematics formulas reflect those or other properties of the original object or its behavior;

e) sequence of electrical signals.

5) Which of the variants relates to the second phase of mathematical modeling?

a) collecting data on the incidence of influenza territory region;

b) finding the incidence of viral infection;

c) collect data on the incidence of influenza City area;

d) using model in practice;
e) none of above.

Practical work:

"Development mathematical model of the human biorhythm"

Properties of functions: A) Domane of the function $y = \sin x$ - the set of all real numbers $D(y) = R$. B) Set of values $y = \sin x$ - interval [1,1]: $E(y) = [-1,1]$. B) Parity and odd of the function: $\sin(-x) = -\sin x$ (the function is odd). D) periodic, with the lowest period 2Π $\sin(x + 2\Pi n) = \sin x$ for any value of X in domain ($n \in Z$).

How to find the period?

Period of the function is 2Π. Thus, in the case: $y = \sin 2x$ the period will be equal

$$T = \frac{2\Pi}{|k|} = \frac{2\Pi}{2} = \Pi$$, k- koefficient at the argument x;

In case $y = \sin\frac{x}{2}$, the period will be equal $T = \frac{2\Pi}{|1/2|} == 4\Pi$

Human biorhythms

Description of the **physical cycle** functions $y = \sin\frac{2\Pi x}{23}$, let's find the period:

$T = 2\Pi/(2\Pi/23) = (2\Pi * 23)/2\Pi = 23$

Emotional cycle: $y = \sin\frac{2\Pi x}{28}$, the period will be equal:

$T = 2\Pi/(2\Pi/28) = (2\Pi * 28)/2\Pi = 28$

Description **intellectual cycle** has formula: $y = \sin\frac{2\Pi x}{33}$

It means that T=33.

What means X?

X - the age of the person. It is determined by *Excel*: you need to subtract from the current date of a person's his or her birth date (using the properties dates).

Computer model

In *Excel* information and mathematical model are combined into a table that contains two areas:
* Output parameters: Constants and variables.
* Estimated data.

	A	B	C	D
1	**Development mathematical model of the human biorhythm**			
2				
3	*Output parameters*			
4				
5	**Constants**	**Days**	**Variables**	
6	Physical cycle	23	Date of birth	20.05.1998
7	Emotional cycle	28	Date of reference	29.02.2016
8	Intellectual cycle	33	Duration forecast	30
9				
10	**Day**	**Physical**	**Emotional**	**Intellectual**

Then use the data obtained from a mathematical model and information model that previously found and make calculations in the *Excel*. Use the properties of the *Excel*: Copy using a marker, absolute addressing, the master functions, charting wizard.

The algorithm in the table

1. Fill the column Day of reference.
2. In cell *A11* enter the serial day - today's date (record date reference copy a month in advance).

3. In cell *B11* enter a formula to describe the physical cycle $y = \sin\frac{2\Pi x}{23}$ (variable X corresponds to the person's age).

=SIN(2*PI()*(A11-D6)/ B6)

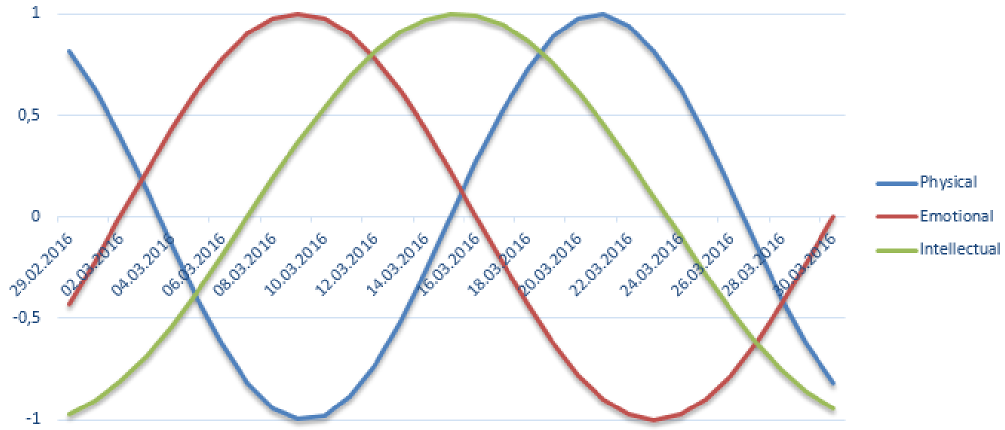
4. In *C11* cell enter the formula to describe the emotional cycle $y = \sin\frac{2\Pi x}{28}$ (variable X corresponds to the person's age).

=SIN(2*PI()*(A11-D6)/ B7)

5. In cell *D11* enter the formula of the intellectual cycle $y = \sin\frac{2\Pi x}{33}$ (variable X corresponds to the person's age).

=SIN(2*PI()*(A11-D6)/ B8)

6. Copy the appropriate formulas in column A, B, C, D to that date.
7. Build a schedule that is a sine wave, reflecting favorable (above the axis OX) and negative (below the axis OX) days of the respective cycles.



8. You should:
• Select the range: the value of all three biorhythms dates.
• Choose Chart Wizard.
• Select chart type - Scatter with smooth curves.
• Format axis: the scale - the price of basic and intermediate divisions - 1 number - the date format, type, alignment - text on back 270^0.

Content of the topic:

MODELS AND MODELING

Mathematical models are mathematical descriptions of real natural objects. There are complicated models from the point of view of obtained results, but simple model in comparison with natural real objects.

Modern science bases on modeling.

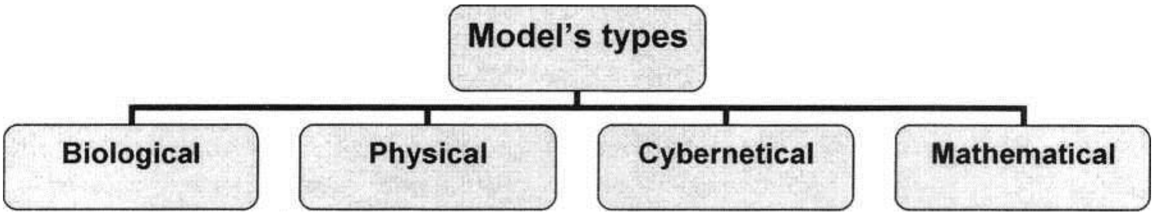
In a research and many design processes often present as extraordinary important stage of modeling:

- for building of airplanes and cars (to investigate behavior of a models in various condition of flaw, in some dangerous or rare situation),
- dams on the river and bays (to investigate behavior of streams in new conditions, load on all parts of dam at varied level of water and wind),
- new construction of highest building and bridges (to investigate behavior of construction and load on all parts of building at varied force and directions of wind) and in many other cases.

Results of work with models are changes of original design, recommends for following work with objects, in some cases - new knowledge.

In biology and medicine models are necessary for predicate behavior of an investigated object in interesting conditions (for example, reaction of human organism on loads which are dangerous for health), peculiarities of process which are inaccessible for usually investigating (for example, blood flaw in a heart).

MODEL’S TYPES



Model is an artificial object with some nature which substitute or reflect investigated object such as investigators can obtain new information about original object during studying of model.

Model is similar to original object only by most important properties. Always model is simpler than object, in majority cases model reflect only little part of object peculiarities. Choose of model type depend on purposes of research.

Investigated object of biology and medicine is live organism that is very complicate system. Model of biological system is:

- a system of equations or formulas, or logical conditions,
- or technical device, which reflect difference sides or peculiarities of original system functioning. Imitation models have very high value for science and practice.

Models give possibilities for the searching of processes in many various conditions, many times, in short time with high speed of modeling processes, without dangerous to the original objects, in situation which don’t accessible to realize in practice (for example, situation of social conflict).

4 main types of models that are wide used biology and medicine.

Biological object model. There are laboratory animals, isolated organs, cells cultures and similar. On these models investigators study common biologic law, medicine effects, results of new methods of treatment and types of surgery. This type of models is most old and very important now.

Physical (analogical) model. There are devices with behavior, which analogue to original object by necessary characteristics. Such device can be mechanical device or electric chain. Examples of such devices are artificial heart, apparatus of art breath for surgery, artificial kidney.

Cybernetic model. It is electronic device or computer programs, which imitate information processes in live organism. Such type of models is basis of robot technique because control of movement and processes of solution taking (part of artificial intellect problem) are main tasks of cybernetic.

Mathematical model. It is system of mathematical functions, equations, and formulas, which describe some characteristics of process or appearance.

Examples of mathematical models are: physical laws (equations used in hemodynamic, astronomy, biochemistry and all other), computer programs modeling animal and human organs and systems (vestibule system, visual system, locomotor analysator, neuron and other).

MATHEMATICAL MODELS

The term model has a different meaning in model theory, a branch of mathematical logic *An artifact which is used to illustrate a mathematical idea* is also called a mathematical model and this usage is the reverse of the sense explained below.

Mathematical model - it is system of mathematical correlations which describe studying process or appearance.

A mathematical model uses mathematical language to describe a system Mathematical models are used in the natural sciences and engineering disciplines (such as physics, biology, earth science, meteorology, and electrical engineering), but also in the social sciences (such as economics, psychology, sociology and political science).

There are several classifications of mathematical models.

Types of mathematical models (some classifications)

Mathematical models can take many forms, including but not limited to dynamical systems, statistical models, differential equations, or game theoretic models.

Mathematical models are material-mathematical and logical-mathematical. Material-mathematical models have mathematical description which identical to physical original. Logical-mathematical models are abstract models which design from signs as logical calculations.

Mathematical models are deterministic and probabilistic (stochastic).

If researcher uses deterministic approach to the problem's solution, he considers that appearances are strictly subdued to certain laws.

A deterministic model is one in which every set of variable states is uniquely determined by parameters in the model and by sets of previous states of these variables. Deterministic models perform the same way for a given set of initial conditions.

If researcher uses probabilistic approach to the problem's solution, he considers that appearances are accidental (casual). Accidental appearance is such, which happens somewhat differently at many times repeats. In a stochastic model, randomness is present, and variable states are not described by unique values, but rather by probability distributions.

Structural models of control processes and models based on artificial intellect (expert models).

These and other types of models can overlap, with a given model involving a variety of abstract structures.

Types of mathematical models of pathological states and processes divide by second classification onto probabilistic and deterministic.

Deterministic Models

Such models meet rarer than probabilistic models. But in biology just using of determining models usually named mathematical modeling.

Deterministic models with uninterrupted space and time (functional dependencies).

Such descriptions use widely in radiology, toxicology, pharmaco-kinetics, at calculation of liquid moving (for example, in blood vessels), at describing of processes of tumor grows, forming of electrocardiogram, metabolic processes, spreading of excitement in muscles and nervous, immune processes and other.

Deterministic models with discrete space and time (logical models).

Logical-informational models are basis of many expert systems. They use logical trees, difference methods of coding, hierarchical schemes, identificators and classificators, sorting algorithms and other.

Such methods of determining are present in many modern medical manuals. There are often "logical trees" for remembering. They are convenient for programming of exert system too.

Special languages and terms systems with them using laws are second type of logic models. For example, it is systematic medical nomenclature SNOMED. They are basis of composing of many information-seeking and experts systems.

Probabilistic Models

Parametric one-measured models based on statistically grounded approximation of empiric distribution. Approximation is executed with using of probabilistic laws, more often normal law.

If you see in the reference book that breath frequency of a child in 1-12 month age equal 35- 48 in minute, this means that breath frequency models by regular law.

If you see in the reference book that body mass of a newborn boys in city X. in 1976-1978 years was equal 3,53±0,47 kg, this means that body mass models by normal law.

Non-parametric one-measured models use in cases when law of empiric distribution is unknown.

Real created models can have probabilistic and deterministic traits: deterministic law of object structure and its behavior are modified in a random way, but random, probabilistic interference has own specific laws.

Structural Models Of Control Processes

There are most part of “bio-cybernetic” models.

Models with unlocked control contours are model without back relations.

Example of such model is classic idea about reflex arc as simple chain consists of afferent link (sensitive cells), central neurons and efferent link (executive organs - muscles or glands).

Models with locked control contours are basis of cybernetics

There are models with back relations. That gives for the system possibility to take into account information about declining of system’s state and results of control.

Models On Basis Of Artificial Intellect (Expert Systems)

There are models having databases and knowledge bases.

In medicine this models are mainly used in diagnostic systems for discrimination of diseases and taking of medical decision.

STAGES OF MATHEMATICAL MODELLING

1) stage is creating of mathematical model basis:
2) accumulation of experimental data about original object;
3) composition of equations described obtained experimental data.
4) stage is checking and correction of a model:
5) finding of number values of models parameters and indexes;
6) solution of equations which are result of the I stage;
7) comparison of solution with experimental data, finding of differences and its causes;
8) correction of the model.
9) stage is investigation of mathematical model and using it in the practice.

Examples of typical biological and medical mathematical models are:

- model of bacterial population grows;
- model of spreading of infection in the limited territory as village, town or city;
- model of blood circulation;
- model of immune system reaction on enemy antigen invasion;
- model of oscillation of animal number in population system “victim-prey”.

MATHEMATICAL MODELS IN BIOPHYSICS

Basic mathematical models represented by one or two equations allowing a qualitative examination, make it possible to describe principal regularities of biological processes: growth restrictions, presence of several stable stationary states, oscillations, quasistochastic regimes, spreading pulses and waves, and the structures inhomogeneous in space.

These models are nonlinear and reflect mathematically the openness of biological systems and their state beyond thermodynamic equilibrium.

This type of models includes the models of growth, interaction between the species, primary processes of the photosynthesis, nerve conductivity, DNA untwisting...

The detalization and identification of these models from experimental data allows the description of real processes in live systems, the examination of their mechanisms, and makes these models heuristic.

The imitation models are constructed for all the levels of the organization of live systems, from the subcellular organelles to the biogeocenoses. The development prospects for mathematical models in biology rest on the use of information technologies.

Using the computers, the imitation models develop vigorously, describing the behavior of a complex system on the basis of the knowledge on its elements and on the regularities of their interaction.

The information technologies allow the integration of knowledge both in the form of mathematical objects and in the form of visual images, which presents a notion on complex laws of the functioning of the regulation laws in alive systems that are difficult to be formalized.

Specificity of mathematical modeling of living systems

Contrary to the diversity of living systems, they all possess the following specific features that must be taken into account in constructing the models.

Living systems are:

1) Complex systems.
2) Proliferating systems.
3) Open systems.
4) Multilevel regulation system.
5) Complex spatial structure.

Complex systems. All biological systems are complex, multicomponent, spatially structured, and their elements possess individuality.

Proliferating systems (capable of self-reproduction) This most important feature of living systems determines their ability to reprocess inorganic and organic matter for the biosynthesis of biological macromolecules, cells, and organisms.

Open systems, steadily passing through themselves the flaws of matter and energy. Biological systems are far from thermodynamic equilibrium and, therefore, are described by nonlinear equations.

Biological objects possess a complex *multilevel regulation system*. In biochemical kinetics, this is expressed by the presence of feedback loops, both positive and negative, in systems. In equations of local interactions, the feedbacks are described by nonlinear equations; their character determines the possibility of the appearance and properties of complex kinetic regimes, including oscillatory and quasistochastic ones.

Feedback

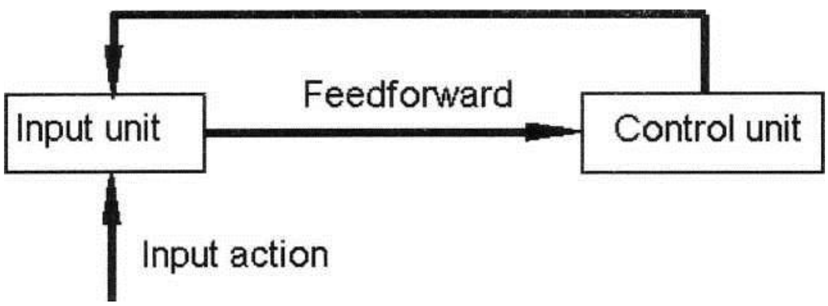


Fig. 1. Simple regulation system.

Feedforward - direct communication.

Feedback - back coupling, feedback coupling. Feedback can be positive (note by + sign) or negative (note by - sign).

System can be stable only in presence of negative feedbacks; otherwise outer influence or inner change will carry to deviation from equilibrium state up to outside conditions of system existence.

Living systems have a complex spatial structure.

A living cell and the organelles in it have membranes, and any living organism contains enormous number of membranes, whose total area reaches tens of hectares. It is natural that the medium inside living systems cannot be regarded as a homogeneous one. The emergence of such a spatial structure and the laws of its formation represent one of the problems in theoretical biology.

The membranes not only single out various reaction volumes of living cells, but also separate the biotic and abiotic (medium). They play a key role in the metabolism selectively, passing through themselves the flaws of inorganic ions and organic molecules. In the membranes of chloroplasts, the primary photosynthesis processes occur: the accumulation of the light energy in the form of the energy of highly energetic chemical compounds; they are used for the synthesis of organic matter and in other intracellular processes.

Mathematical models of the processes in biological membranes comprise a significant portion of mathematical biophysics.

Existing models are mostly presented by the systems of differential equations.

However, it is obvious that continuous models cannot describe in detail the processes that occur in such individual and structured systems as living systems.

As computational, graphical, and intellectual facilities of computers develop, the imitation models, based on the discrete mathematics, play ever increasing role in mathematical biophysics.

Imitation models of concrete complex living systems, as a rule, take into account all available information about given objects. The imitation models are employed to describe the objects of different organization levels of live matter: from biomacromolecules to biogeocenoses. In the latter case, the models must include the blocks describing both living and «inert» components.

Models of molecular dynamics are a classic example of imitation models, in which the coordinates and impulses of all atoms that compose a biomacromolecule and the laws of their interactions are prescribed.

In mathematical biophysics, as in any science, simple models exist that are liable to analytic examination and possess properties that allow a whole spectrum of natural phenomena to be described. Such models are called basic.

In physics, harmonic oscillator (a ball, material point, on a spring without friction) is a basic model.

Despite enormous diversity of living systems, one can single out some of their inherent most important properties: growth, self-restriction of growth, ability to switching, i.e., the existence of two or more stationary regimes, self-oscillating regimes (biorhythms), spatial nonhomogeneity, and quasistochasticity.

All these properties can be demonstrated on comparatively simple nonlinear dynamic models, which play the role of basic models in mathematical biology.

Unlimited growth. Exponential growth. Self-catalysis (Auto-catalysis)

The rate of growth is proportional to the population numbers, no matter is this a hare population or a population of cells; this is one of fundamental assumptions underlying all models of growth. For many one-cell organisms or for the cells contained in cellular tissues, the proliferation means simple division, that is, doubling the number of cells for a certain time interval called the characteristic division time. The proliferation of plants and animals, whose organization is complex, follows more complex laws; however, in the simplest model, one may assume that the proliferation rate of a species is proportional to the numbers of this species. This is written mathematically with the use of a differential equation linear with respect to a variable x characterizing the numbers (concentration) of individuals in population:

$dx/dt = rx$ (1)

Here, r can be, in general case, a function of both the numbers and time or depend on other exterior and interior parameters.

The law (1) was formulated by Thomas Robert Malthus (1766-1834) in his book "On the Growth of Population" (1798). According to (1), if the proportionality coefficient r = const (as Malthus assumed), then the numbers grow exponentially and without limits:

x=x0ert; x0-x (t=0) (2)

For most populations, the limiting factors exist, and the growth of population terminates due to a variety of reasons. Human population is the only exception: during the whole historical time, it increases even faster than exponentially. The investigations performed by Malthus exerted a great influence both on economists and biologists, in particular, Charles Darwin analyzes the Malthus theory in his diaries in detail. Darwin understands the straggle for existence in real living nature as one of the causes for breaking the Malthus law. The law of exponential growth is valid at a certain growth stage for the cell populations in a tissue, for alga or bacteria in a culture. In models, the mathematical expression that describes the increase in the rate of change of a quantity is referred to as autocatalytic term (the catalysis means a modification of the reaction rate, usually the acceleration, with the help of substances that do not participate in the reaction), and the autocatalysis means the "self-acceleration" of a reaction.

Bounded growth. The Verhulst equation.

The Verhulst model (1848) is a basic model that describes the limited growth:

dx/dt= rx(1-x/K) (3)

The parameter K is called the "population capacity" and expressed in the units of numbers (concentration); it is of system character that is, determined by a number of different factors. Among the latter, these are the limitation to the amount of substrate for the microorganisms, space available for a cell population in a tissue, the food base, or the refuge for superior animals. Diagrams of the dependence of the right-hand side of Eq. (3) on the numbers x and on the population numbers in time are presented in figures below.

The examination of a discrete analogue of Eq. (3) in the second half of the 20th century has revealed its quite new and wonderful properties. Consider the population numbers at sequential moments, which corresponds to a real procedure of counting the species (or cells) in a population. The dependence of the numbers at a time step numbered n+1 on the numbers at the preceding step n can be written as

Xn+1=rXn(1-Xn) (4)

The behavior of the variable xn in time as dependent on the parameter rcan be characterized not only by unbounded growth, as it was in the continuous model (3), but also be oscillating or quasistochastic, as it is shown in figure below on the left.

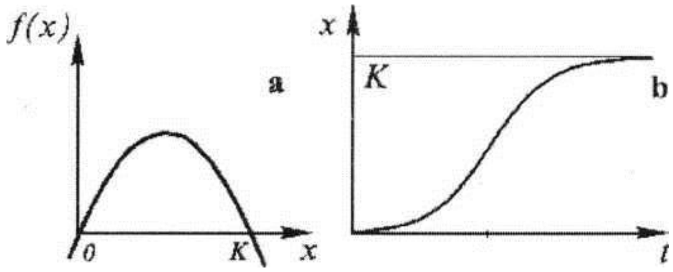


Fig.2. Limited growth.

When the diagram on the left becomes steeper, the stable equilibrium passes into stable cycles. As the numbers increase, the cycle length increases, and the values of numbers repeat in 2, 4, 8, ... 2n generations. At the value r > 2.570, the chaotization of solutions happens. At r sufficiently large, the population dynamics demonstrates chaotic spikes (outbursts of the insect numbers). Equations of this type describe the numbers dynamics of seasonally proliferating insects with not overlapping generations.

Fig. (a) dependence of the numbers at subsequent step on the numbers at preceding step and (b) behavior of the numbers at different values of the parameter r for the discrete model of logistic growth (3): (1) bounded growth; (2) oscillations; (3) chaos.

For small r (r <3), the population number tends to a stable equilibrium.

The discrete description proved to be instrumental for the systems of most different nature.

The representation of dynamic behavior of a system at a plane in the coordinates [xt, xt+T] allows one to determine if the observed system is oscillatory or quasistochastic.

For example, such representation of the cardiogram data made it possible to establish that normal systole s of human heart are of irregular character, while in the period of breast-pang fits or in a preinfarct state, the systolic rhythm becomes strictly regular. Such a «rigid» regime "aggravation" is a protective reaction of organism in a stress situation and points to the danger to the life of system.

Competition. Selection

Biological systems interacts with each other at all levels, be it the interaction of macromolecules in the process of biochemical reactions or the interaction of species in populations.

The interaction can occur in structures, and then a system can be characterized by a certain set of states, which happens at the level of subcellular, cellular, and organism structures. Kinetics of the processes in structures is described in mathematical models, as a rule, by the systems of equations for probabilities of the states of complexes. In the case, when the interaction occurs at random, its intensity is determined by the concentration of interacting components and by their motility, the generalized diffusion. These are the concepts that are conventional in the basic models of the species interaction.

The monograph by Vito Volterra "Mathematical Theory of the Struggle for Existence" (1931), in

which mathematical models of the species interaction were considered, became a classical book. In this book, properties of biological objects and their interactions are postulated in a mathematical form and then examined as mathematical objects.

This effect of grows of predator quantity in condition of victim grows was predicted by the model "predator-victim" proposed by Volterra.

It was confirmed: when in the years of the First World War (and immediately after) the fishing intensity dropped sharply, the relative portion of predator fish in a catch had increased.

Volterra assumed, by analogy with statistical physics, that the interaction intensity is proportional to the probability of meeting (collision probability for molecules), that is, to the product of concentrations.

These and some other assumptions, made it possible to construct a mathematical theory of the interaction between populations of the same trophic level (competition, symbiosis) or different trophic levels (predator-pray, parasite-host).

Other examples of classic models are:

Constraints with respect to a substrate. The models of Monod and Michaelis-Menten Shortage of food is one of the limits for growth (in microbiological language, substrate limitation). The growth rate increases proportionally to the substrate concentration, and in the abundance of substrate, arrives at a constant value determined by genetic capabilities of population.

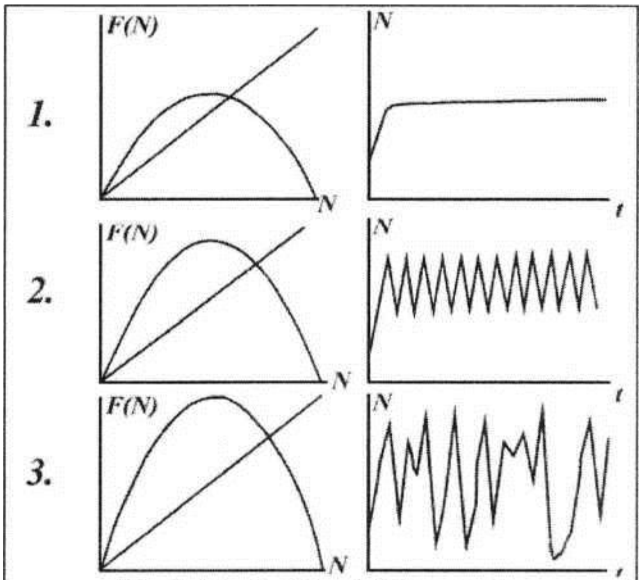


Fig.3. Limited logistic growth.

Classic Lotka-Volterra models

The simplest nonlinear models of the interaction between chemical substances in the Lotka equations and between species in the Volterra models made it possible, for the first time, to understand that self-oscillations are possible in an energetically rich system due to specificity of the interaction between its components.

Models of the interaction between species

In the middle of the 20th century, the interest to ecology and fast development of computing facilities, which made it possible to solve and examine the systems of nonlinear equations, stimulated the development of population dynamics.

Models of the enzyme catalysis

Enzymes are highly specialized catalysts accelerating the rate of biochemical reactions by hundred thousand and million times. Any enzymatic transformation starts with the fixation of substrate molecules by an active center of enzyme and completes by breaking these fixations.

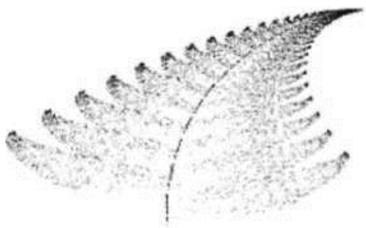
Model of a continuous microorganism culture

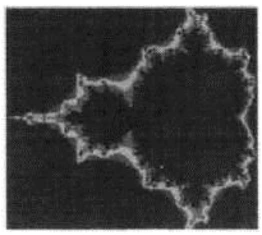
Microbiological populations are a good experimental object for verifying ideas and results of both ecological and evolutionary ideas. In biotechnology, for calculating the optimal cultivation regimes, the formulas are applied that take into account other peculiarities of the metabolism of the microorganisms themselves, and also of the conditions of their cultivation.

SOME OTHER MODELS

Artificial Life (ALife), as an area of investigations, took its form in the late 1980s. ALife “organisms” are man-made, imaginary entities, living in computer-program worlds. ALife evolutionary modeling is currently developing field of evolutionary investigations.

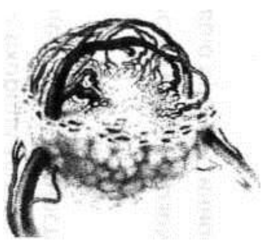
Fractals in modeling





A fractal is an object or quantity that displays self-similarity, in a somewhat technical sense, on all scales. The object need not exhibit exactly the same structure at all scales, but the same "type" of structures must appear on all scales.

Illustrated above are the fractals known as the Gosper island, Koch snowflake, box fractal, Sierpinski sieve, Barnsley's fern, and Mandelbrot set.



Geometrization of brain theory

The complex arbor of a dendritic tree could be mathematically equated with simple Euclidean geometrical primitives (cylinders) provided that the bifurcation of the branches follawed Rail's "three halves rule"; i.e. that the diameter of the "mother branch" R and those of the "daughter branches" robeyed the branching power of n=3/2: R3l2 = r13/2 + r23/2.

Self-Similarity - neuron growth

A main principle of fractals, that the whole is similar to its parts, is qualitatively demonstrated for classical Golgi-stained Purkinje cells (from Cajal 1911).

Similarity of the arborization of individual cells is shown in A (compare the patterns of two Purkinje cells). A separated Purkinje cell is shown in B, where branchlet of the top right corner is framed.

This part magnified (C) displays a qualitative similarity of arborization of the entire neuron (B).

Note the limitations and imperfections inherent in using drawings of classic Golgi-stained material.

The feasibility of fractal models to reduce and at the same time to conserve complex arborizations.

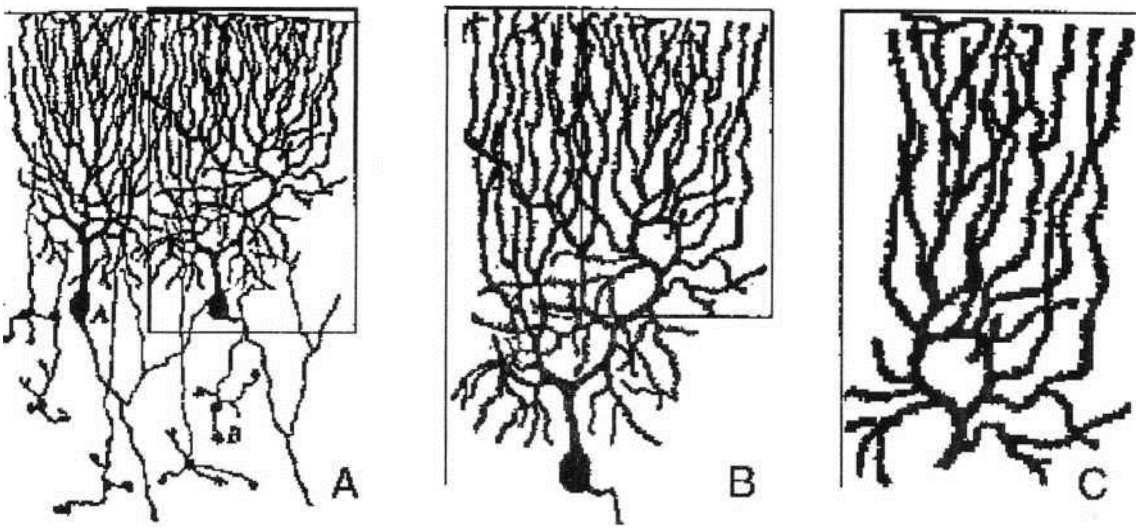


Fig.4. Purkinje cells on different levels of observations (magnification).

Tasks for self-check:

Task 1:

1) What was the name of the first mathematical model proposed in biology?
a) Camus "Elements of Physical Biology";
b) Volter "Predator - prey";
c) Lotki "Physics";
d) Lotki "Biology";
e) Virt "Elements of Physical Biology".
2) What usually used in the models?
a) a system of linear equations
b) a system of differential equations
c) integrals
d) derivatives
e) logarithms
3) What software tools help to create tabular model?
a) MS Word
b) Paint
c) MS Excel
d) MS Access
e) All of these
4) What models are aimed at simplifying the complex nutrient chains to their basic components or trophic levels?
a) environmental
b) math
c) physical
d) virtual
e) models in ecotoxicology
5) Schedule of trains can be presented in the form of charts, tables, text, because it is ...
a) specialization
b) informational model
c) physical model
d) biological model

e) virtual model

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Basic.

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Additional.

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4. www.cochrane.ru (Розділ Кохранівського співтовариства)

The methodical guidance has been completed by **S.Y. Olenets**