Theoretical and Experimental Approaches to Study of Biological Objects by Mathematical Methods Using the Example of Hormone Production in the Thyroid Gland

Olha Ryabukha (MD, PhD in Medical Sciences, Professor, Lviv Medical University, Ukraine)  
Corresponding author: Olha Ryabukha

Received: June 18, 2024  
Published: July 10, 2024

Abstract. The study of any biological object is a complex process that involves a number of successive stages, one of which tools can be a specially created expert system. It is advisable to present the conclusion about the studied biological object in clear forms of expression – quantitative or binary, which are the results of the practical application of the principles of absorption by some researched factors of others, a compromise between them or the prevailing alternative of the studied properties. The involvement of mathematical technologies in the identification and explanation of the regularities of the activity of biological objects requires the display of the results of their research using a mathematical language. This makes it possible to establish regularities in the course of biological processes and predict their consequences. Since any living system is formed from a large number of elements, the organism has a complex hierarchy of structural and functional levels of organization. A mandatory prerequisite for the activity of a biological system is a variety of states, each of them being characterized by its own characteristics – markers of change, which, according to the degree of completeness of the one state transformation into another, should be divided into markers of primary changes, markers of prevailing majority changes, and markers of final changes. Comprehensive application of the Semiquantitative analysis of electronograms according to Ryabukha O. (2000) and her method for determining the profiles of hormonopoietic cells’ special capacities (2003) when studying the cytophysiology of the thyroid gland in normal and pathological conditions, it is possible to determine the specific link of the follicular cell’s specialized activity, in which there was a violation of hormonopoiesis, and to assess its intensity. The developed Conceptual apparatus of functional connections between organelles of hormone-producing cells when studying them by the Method of correlation analysis by creating intra- and intersystem correlation portraits reflects the features of mutual influences and interdependencies, which deepens the understanding of the intimate mechanisms of hormonopoiesis.

Keywords: biological system, expert systems, thyroid gland, follicular cell, pre-disease, markers of changes, hyperthyroidism, correlation portrait, nodal dots.

Introduction. The mathematically based stage of research in biology and medicine is a qualitatively higher stage of learning the patterns of biological systems’ vital activity. The use of mathematical methods, in particular mathematical modeling, for the study of biological objects (cells, tissues, organs or the whole organism) is an urgent need of modern biomedicine [1,2]. This is due to a set of reasons, the main ones of which are the expansion of the possibilities for searching and identifying the regularities of the studied objects’ functioning with their analysis. Since the mathematical approach permits to reveal the dependence of some phenomena on others, research using mathematical models is especially important for establishing a diagnosis, choosing treatment measures, predicting the course of diseases, etc. [3–7]. At the same time Torres N.V. & Santos G. (2015) rightly point out that mathematical modeling of the biological systems’ activity is a very complex process [8]. By their nature, biological systems consist of many elements that are closely interconnected by processes and interactions that occur at different levels of their organization (molecular, cellular, tissue, whole organism, and ecological) and are realized in an open system in which there are multiple gradients far from thermodynamic equilibrium. A very complex nonlinear dynamics between the elements of the biological system does not allow them to be subjected to accurate quantitative and mathematical description. In this case, it is necessary to update the views on the cell as a non-entropic biological object, which activity should be studied on the basis of specially developed expert approaches [9]. In particular, the Nobel laureate prof. Schrödinger E. pointed to the method of knowledge systematization (“synthesis of facts and theories”), which he
considered a promising field of such research and an important method of learning integral knowledge [10]. According to Mintser O.P. & Babintseva L.Y. (2022) further progress of medicine in solving the problems of non-infectious diseases can be achieved by rethinking modern fundamental knowledge and creating the latest promising scientific fields for their solution [11].

In view of the above, we consider the cell as a complex self-regulating cybernetic system, which is constantly subject to an array of influences that initiate various changes in it. Initiating influences can be schematically divided into two main groups – external and internal, while internal influences can be implemented by other systems of the same body or other structures of the same organ. Since the cell is usually subject to several influences or an array of influences, they can be mutually reinforcing, mutually weakening, or independent of each other, that is, implemented in isolation from each other [12]. Certain specialized groups (clusters) of cell organelles, which in the cell implement a certain direction of its activity, are the points of application of the initiator influences’ action [13]. Electron-microscopic morphological signs of influence on the appropriate cluster of ultrastructures are changes in its elements: number, structure, electron density, localization in the cell, relationship with other elements of the same cluster or with elements of other clusters. Given the interdependency and interdependence of structure and function, morphological changes are also functional at the same time. Then the analytical study of the morphological features of one organelle permits to determine its functional state and functional capacity, and the generalization of morphological changes of cluster elements indicates the main direction of influence of a certain factor on the entire cluster. Since several organelles or structural components of an organelle are implementers of one cell activity’s field, the effects of one direction of action, but different in strength, nature, dosage, etc., can selectively act on different components of the same cluster or cause different changes in the elements of the cluster.

**The purpose of the study** was the analytical summarization and systematizing of information from the scientific literature regarding the possibilities and prospects of applying mathematical methods for analyzing the results of studying complex multilevel biological systems and their experimental implementation in the practice of studying hormone-producing cells.

**The objects of the study** were mathematical methods used in studying the activity of biological systems. **The subjects of the study** were peculiarities of using quantitative, binary, and qualitative data when studying the activity of a biological system using the example of the thyroid gland’s follicular cells.

**Materials and methods.** The material of the practical study is electronograms of male albino rats’ thyroid glands, made according to routine methods. The methods of the study were analytical review of scientific literature on the research topic using the Scopus, Web of Science databases, other peer-reviewed publications, electron microscopy, Semi-quantitative analysis of electronograms according to Ryabukha O., and her method for determining the profiles of hemopoietic cells’ special capacities [14], Pearson correlation analysis [15], the Portraits Creating Method by correlation analysis of hormone-producing cells data [16,17].

**Statement of the problem and justification of the work’s topic.** The general theory of systems [18] is one of the foundations for the development of cybernetics and informatics, the achievements of which can be applied in almost all fields of medicine. The study of any biological object takes place in several successive stages: the initial accumulation of empirical data about the object under study, their description, the primary ordering of the information obtained, its systematization. Collectively, the indicated stages of cognition are the basis for forming ideas about the studied object and creating hypotheses and theories about its activity. In his Modern Theories of Development (1933), Ludwig von Bertalanffy argued that “all vital processes are so organized that they are directed to the maintenance, production, or restoration of the wholeness of the organism.” [19]. However, a holistic view of a biological object as a complete system is formed only after the involvement of appropriate mathematical methods, through which it is possible to find out the main aspects and regularities of its functioning [20]. An expert system can be a tool for in-depth research of any biological object, the development of which usually consists in the sequential execution of such stages as identification, conceptualization, formalization, implementation, testing, experimental approval.
At the identification stage, the purpose of the research is clarified and the tasks facing the researcher are determined, there is an awareness of what needs to be done and what resources need to be involved to solve the tasks. At the stage of conceptualization, an in-depth analysis of the studied problem is carried out, the most important (priority) study objects are determined, their essence is understood, and methods of problem solving are specified. The formalization stage is devoted to the presentation of all key concepts and relations in some formal language that already exists or is specially created [21-24]. At this stage, measures and means of solving the task, ways of solving it in the chosen formal language and obtaining results are determined. At the implementation stage, an appropriate expert system [25] is created, which is improved, modified, and supplemented at further stages of testing and experimental approval. The process of creating expert systems is not strictly regulated: it is possible for certain stages to drop out, as well as violation of their sequence.

The study of a biological object through the mediation of expert systems permits to establish its features, and after systematization of the obtained information, to have more complete knowledge about it. At the same time, the degree of knowledge on a biological object is always incomplete, because each biological system not only has a complex structure and consists of many hierarchical subsystems, but also because each of these structures is multivariate regarding the field of activity. It is important to note that the course of physiological processes depends on the conditions in which the vital activity of the system or the entire object takes place: the norm or compensatory and adaptive reactions or pathology. It is obvious that under conditions of normality or pathology, the characteristics, or parameters of the same physiological process in the same biological object will differ among themselves.

The modern stage of scientific medical knowledge is no longer possible without theoretical development, creation, and practical testing of various models of the pathological process development, its course, prediction of consequences, establishment of efficacy criteria for the application of various treatment methods. This presupposes the creation of appropriate expert information and logical schemes or systems, which are designed to investigate a problem or phenomenon, establish contradictions in them and propose ways to overcome contradictions. A conclusion about the state or activity of a biological system is usually expressed in a linguistic (fuzzy, non-numerical) form. For further processing, analysis, and generalization of the results, it is advisable to bring the conclusion to a non-linguistic (clear, digital) form, which will determine the possibility of quantification. Variants of a clear form can be both a quantitative (digital) and a binary (sign is present/sign is absent) form of expression, and the analysis process itself should be carried out through the involvement of co- and counter-factors that permit to characterize the biological object in many ways. The main principle used in determining the interaction of two factors of different strength, which are in a relationship of significant contradiction, is the principle of weaker signs’ absorption by stronger ones. In the presence of two factors of equal strength, it is possible to use the principles of compromise or the prevailing alternative. The application of the compromise principle involves forming one instead of two opposing judgments that can explain the information obtained, summarize them, and remove contradictions between them. For example, during a morphometric study of the thyroid gland’s follicular epithelium, an increase in the height of follicular thyocytes, which is inherent in iodine deficiency states, is a sign of a false increase in the hormonal activity of the organ, and a compensatory-adaptive mechanism, which indicates that the process occurs under conditions of functional stress of the cell. Understanding this permits morphometric signs of gland hyperfunction to be considered manifestations of its hypofunction, and such morphometric hyperthyroidism to be defined as functional hypothyroidism. According to the principle of the prevailing alternative, preference is given to the judgment that is the closest to the corresponding pole of evaluation (comparison). For example, the detection in iodine-deficient hypothyroidism during the morphometric examination of the thyroid gland tissue of single thyocytes that have a normal height is not diagnostically significant, since the vast majority of the examined cells are tall. However, premature neglect of information that cannot be logically understood and generalized at this stage of research can cause the loss of important information, which ultimately leads to incorrect conclusions about the biological system being studied.
The results of scientific research should be based on mathematical calculations and broad generalizations. At the same time, given the multidimensionality of any biological object and the presence of different systems of knowledge about them, a slightly different interpretation of the information obtained during research is possible. In this case, the research results must be presented using scientific language, which consists of two parts. The main is the informative part – it contains information, which can be an unclassified set of factors necessary for a certain field of knowledge. The second part of the scientific language is a corresponding calculation, which is a concise form of expressing connections, rules and conclusions that allow transitions from one linguistic transformation to another. The introduction of the means of mathematical language into the language of biomedicine significantly expands the possibilities of medicine, as it has a significant functional load, which consists of:

- description and systematization of knowledge;
- obtaining comparable results;
- verification of initial concepts and functional dependencies between them;
- formation of principles in a specific field of medicine.

This provides the means not only for deepening the statements that already exist, but also the opportunity for various predictions. Thus, the use of mathematical language ensures the performance of certain cognitive functions and the acquisition of new knowledge about the essence of the objects of a certain science.

The process of learning about the activity of a biological object takes place in several stages. The beginning of the study involves the accumulation, description, and initial systematization of information on its morphology and functioning. The obtained data are subject to further in-depth systematization and generalization, on the basis of which certain concepts regarding its functioning are created. Since anybody consists of a huge number of elements, each of them having its own morpho-functional characteristics, the properties of each element can be described using certain parameters and variables, which permits establishing the presence of certain dependencies between them. Then the main task of diagnosing the state of the biological system will be to establish quantitative relationships between the set of detected signs and a certain state of the system, which must be carried out taking into account the informativeness of each sign and their combinations. Additionally, adequate, and inadequate changes in relation to the environment constantly occur in the biological system, all parameters of its physiological functions change in a wide range. Given this, they can characterize both a state of dynamic equilibrium of a normal system in the so-called “health range” and a severe pathological process with deep structural changes in organs.

One of the mandatory prerequisites for the functioning of a biological system is its diversity, that is, the number of states that the system can acquire under certain conditions. Diversity is one of the most important properties of all living systems, as it determines the degree of their organization complexity. Then each of the elements of the biological system can consistently be in the following states:

- normal life activity;
- state of excitement;
- state of functional tension;
- state of emergency;
- disorders of normal life mechanisms and “functional” changes;
- breakdown of normal life mechanisms and “organic” changes.

The diagnosis of a biological system involves the establishment of quantitative relationships between a set of detected signs and a certain state of the system, taking into account the informativeness of each detected sign and their combinations. A thorough study of a biological system’s organization should include the study of its structure and function not only under conditions of homeostasis (norm) or pathology, but also under in-between borderline (transitional) conditions. It is known that each biological system has certain adaptive reserves that ensure its full functioning under normal conditions and permit the implementation of life processes in the event of homeostasis violation. The loss of these reserves leads to the formation of new qualitative processes and states, in
particular, pre-diseases and diseases. The application of a mathematical approach permits to establish certain characteristics of a biological system in a state of functional equilibrium and to reveal its potential. This, in its turn, leads to the identification of critical points in the course of the biological process, in-depth characterization of the adaptive and compensatory capabilities of the system, establishing signs of the probability of the pathological process reduction or signs of the inevitability of its progression. In this case, normal and pathological processes have a number of common features of a qualitative and quantitative nature, which ultimately determine the mode of functioning of the biological system that is most appropriate for its structure and potential capabilities.

Their markers are a material reflection of the changes that occur in the biological system under the influence of various factors. For a versatile characterization of the process, forecasting its course or possibilities of the studied biological system’s functioning, it is advisable to divide the markers of changes [26] into markers of primary changes, markers of the prevailing majority of changes, and markers of final changes (Table 1).

**Table 1. Gradation of markers of changes in the state of the biological system.**

<table>
<thead>
<tr>
<th>Type of marker</th>
<th>Pathology process stage</th>
<th>Characteristics of the biological system’s state</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marker of primary changes</td>
<td>Initial (pre-disease)</td>
<td>• Tension state:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>− violation of primary functional balance;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>− functional tension;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>− violation of primary adaptation.</td>
</tr>
<tr>
<td>Marker of prevailing majority changes</td>
<td>Pathological process as it is (disease)</td>
<td>• Emergency state:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>− initial functional imbalance;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>− deepening system’s deregulation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• “Functional” changes:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>− forming system’s disorganization.</td>
</tr>
<tr>
<td>Marker of final changes</td>
<td>Final (recovery or transformation into a chronic form)</td>
<td>• “Organic” changes:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>− final change of primary qualities;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>− acquiring new qualities:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>~ forming new state of functional balance,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>~ forming adaptation to new conditions of existence;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>− consolidation of acquired new qualities and formation of a new system.</td>
</tr>
</tbody>
</table>

Markers of primary changes appear at the initial stages of the pathological process and indicate a violation of the primary functional balance. As the duration of the process increases, so does the number of parameters of the biological system that are out of primary functional equilibrium. This disrupts the adaptation of the system to the conditions of existence and causes the appearance of signs of disordered relationships between its elements. When shifts in the system quantitatively outweigh the state of primary functional equilibrium, markers of prevailing majority changes (significant changes) appear. Markers of final changes in the state of the biological system appear at the stage of irreversible changes and completion of the process. In this aspect, it should be noted that conditions whose characteristics are beyond the parameters of the adaptation norm for certain hierarchical levels should be considered pathological. Since any pathological process is always a generalized result of changes in the regulatory systems of its own and higher hierarchical level, the study of processes occurring in living systems should be carried out taking into account the level of the studied system, properties and signs of its structural elements and features of regulatory and adaptation systems of
higher hierarchical levels. At the same time, the reduction of the pathological process is also a series of consecutive stages, each having its own characteristics with its own markers of change.

Studying the activity of biological systems is a complex cognitive process that requires compliance with certain basic requirements. As it was mentioned, given that the body is formed of a huge number of elements, each having its own structure and function, any living system can logically be classified as a class of supersystems with its own hierarchy [27,28]. The sequence of structural and functional connections in a body can be displayed as follows: organelle → cell → tissue → organ → morpho-functional system → functional module → organism. Unlike the morpho-functional system, which involves the interaction of organs with closely related functions (for example, the Cardiorespiratory or Genitourinary System), the organs that make up the functional module may belong to different anatomical or physiological systems, but have a common direction of action (functional task), which is caused by common metabolic transformations. For instance, since tyrosine is a substrate for the synthesis of both thyroid and steroid hormones, and the liver is the site of their metabolism, we proposed to combine the thyroid gland, adrenal glands, and liver into the single Thyroid-adrenals-liver Functional Module [29,30]. In general, it is advisable to present the structural hierarchy of biological objects at three levels of organization (Table 2).

Table 2. Hierarchical levels of biological systems’ organization.

<table>
<thead>
<tr>
<th>No.</th>
<th>Organization level</th>
<th>Representative of the hierarchy</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Organelle–cellular</td>
<td>Cellular organelle, Cell</td>
</tr>
<tr>
<td>II</td>
<td>Tissue–organ’s</td>
<td>Specialized tissue, Organ</td>
</tr>
<tr>
<td>III</td>
<td>System–somatic</td>
<td>Morpho-functional system, Functional module, Organism</td>
</tr>
</tbody>
</table>

The basic level of structural organization is the level of cellular organelles, and the highest is the integrative level of the organism. In this case, changes that occur at the cellular level can be leveled by regulatory mechanisms inherent in higher levels. It should be noted that the study of each level of a biological object’s organization can take place on the condition that its properties and characteristics are known, and the elements of the system remain unchanged during the study.

Results and discussion. A biological system at any level of hierarchical organization is characterized by the following main features: 1) certain properties of elements; 2) the intensity of element manifestations; 3) the type of associations between elements; 4) the close of associations between system elements [31]. When studying a biological system, changes in the properties of its elements and the types of connections between them can be displayed in the form of mathematical functional dependencies [32]. This permits the quantitative approach to the study of phenomena to be transformed into the definition of their qualitative characteristics, and, therefore, variables. In view of the above, the need to formalize various life processes of biological objects increases significantly. As an example, we will give the formalization of the state of hormone-producing cells during the study of the thyroid gland by the method of electron microscopy. Although it is possible to study in detail the state of cellular organelles and the dynamics of their reorganization under various conditions of life (functional balance, disruption of functional balance under the influence of various factors, pathological changes, etc.), the main approach to studying electronograms of cells is a linguistic description of the electron microscopic picture, which to some extent is a manifestation of empirical study method’s predominance.

The approaches developed by us to formalize the morpho-functional state of the organelles of hormone-producing cells are particularly informative when studying the influence of various substances or environmental factors [33]. We have added knowledge about the main mechanisms of hormonopoiesis in the thyroid gland and their morphological manifestations [14]. In general, it can
be said that any cell of the hormone-poietic series is capable of fully functioning if the following basic prerequisites are simultaneously present:

1) organelles that carry out the synthesis of a hormonal substance;
2) organelles that secrete the produced hormonal substance;
3) organelles with the help of which the hormonal product enters the capillary bed;
4) organelles that provide energy for these processes.

Each of these specified factors of the hormone-producing cell’s functioning is proposed to be qualified as an “capacity”. Given the fact that the realization of capacities is carried out by groups of certain, functionally relevant specific organelles and their elements, it is possible to assess the degree of manifestation of the characteristic features of each of these groups’ elements. Research is carried out according to the developed algorithm: first, in accordance with the author’s Method for determining the profiles of hormonopoietic cells’ special capacities organelles are clustered according to the directions of their specific activity [34]. In particular, the synthetic capacity of the follicular cell is characterized by the degree of electron density of cytoplasm, the state of the rough endoplasmic reticulum and the Golgi body, the number of free and fixed ribosomes and polysomes [17,35]. The secretory capacity of the follicular cell is evidenced by the features of the microvilli of the apical cell membrane, lysosomes and secretory vesicles, and the degree of electron density of the intrafollicular colloid [36]. The characteristics of the pericapillary space, the condition of endotheliocytes and perifollicular capillaries testify to the state of the thyrocyte’s transport capacity [37,38]. Extended characteristics of mitochondria indicate the state of energy capacities’ profile [39].

After that, the author’s Method of semi-quantitative analysis of electronograms in each cluster determines the number, state, and mutual location of its elements. The presence of signs and the degree of their manifestation are assessed using a scale developed by us: “0” – no sign; “1” – manifestation of the symptom is low; “2” – manifestation of the symptom is moderate; “3” – manifestation of the symptom is high; “4” – manifestation of the symptom is very high (maximum). Assessment of the state of the cell is carried out by comparing the number and state of the studied cluster’s elements with their state in standard cells (normal and uncorrected pathology). The degree of manifestation of any signs in the follicular cells of a normal thyroid gland is estimated at 4 points (Table 3). To assess the synthetic activity of follicular cells with very high activation of hormonopoiesis by inorganic or organic iodine, an increase in the number of ribosomes up to 8 points (200%) is possible.

**Table 3.** Scale of transformation of qualitative results of electronograms’ semi-quantitative analysis into quantitative indices.

<table>
<thead>
<tr>
<th>Degree of symptom manifestation</th>
<th>Degree of symptom manifestation assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(percentage)</td>
</tr>
<tr>
<td>“0”</td>
<td>0</td>
</tr>
<tr>
<td>“1”</td>
<td>25</td>
</tr>
<tr>
<td>“2”</td>
<td>50</td>
</tr>
<tr>
<td>“3”</td>
<td>75</td>
</tr>
<tr>
<td>“4”</td>
<td>100</td>
</tr>
</tbody>
</table>

An important task for diagnosing the morpho-functional state of a hormone-producing cell is to establish quantitative relationships between the set of detected signs and a certain state of the system, taking into account the informativeness of each sign and their combinations. Then the quantitative (digital) results obtained by analyzing the cytophysiological characteristics of follicular cells of a certain capacity (direction of activity) can be subjected to further mathematical processing using factor, regression, or correlation analysis. When applying Pearson’s correlation analysis [40], it is advisable to display the results in the form of correlation portraits – digital tables or their graphic equivalents [16]. The correlations traced between the elements of one capacity profiles of a hormone-producing cell (cluster) are marked as intra-system, and between the elements of different clusters – as inter-system. The study of intrasystemic connections in correlation portraits begins with the
theoretical determination of those organelles that are functionally significant for the implementation of the investigated direction of activity of the hormone-producing cell. Due to their functional significance, these “supporting” organelles are common to all correlation portraits of the cluster. When studying the synthetic activity of a hormone-producing cell, they are moderately expanded elements of the rough endoplasmic reticulum and Golgi body, a moderate number of ribosomes (free and fixed). In the study of secretory activity – a moderate electron density of follicular colloid, a moderate number of apical microvilli with their moderate length and compactness of location, a moderate number of lysosomes, a moderate number of secretory vesicles with their location in the apical pole of the cell, the presence of a topographic connectivity between lysosomes and secretory vesicles. When investigating the transport capacity, the “supporting” organelles in the correlation portraits are the moderate tortuosity of the basal cell membrane, the moderate width of the pericapillary space, the unchanged (normal) state of the endotheliocytes, and in the perifollicular capillary lumen without changes (moderate electron density, alone erythrocytes (0-2) or erythrocytes in group (2-4) without adhesion, etc.). When examining the energy capacity, there is a moderate number of mitochondria, the presence of a topographic connectivity of mitochondria with the rough endoplasmic reticulum and the Golgi body, the absence of degenerative changes in mitochondria, a clear outline of the mitochondrial cristae, a moderate number of ribosomes on the mitochondrial cristae, a moderate electron density of the mitochondrial matrix.

When creating a specific correlational portrait, its individual correlational connections traced between its elements – “actual” connections were determined. Analyzing the “actual” relationships of a correlation portrait takes place in several stages: identifying its “supporting” and “actual” elements in the portrait, determining whether or not they coincide, determining the presence or absence of correlations between the elements of the cluster under study, analysis of these connections and their closeness (very high, high, marked, moderate) [31], determination of “nodal dots” as places of intersection of correlational connections between organelles [41]. The step-by-step implementation of the specified algorithm makes it possible to both specify and generalize the results of the search for interrelationships between the organelles of the cluster. We are the first to establish that the nodal points of the correlation portraits are the mathematical results of changes in the cells. This makes them a source of important information for cytophysiology. For example, we present correlation portraits of the transport capacity of follicular cells of the thyroid glands in male albino rats whose iodine deficiency (Fig. 1) was corrected with a small dose of organic (Fig. 2) and a small dose of inorganic (Fig. 3) iodine.

![Fig. 1. Graphic representation of the nodal dots transport capacity correlation profile structure of the male albino rats’ follicular cells in the conditions of alimentary iodine deficiency.](image)
Fig. 2. Graphic representation of the nodal dots transport capacity correlation profile structure of the male albino rats’ follicular cells when taking small dose of organic iodine in conditions of alimentary iodine deficiency.

Fig. 3. Graphic representation of the nodal dots transport capacity correlation profile structure of the male albino rats’ follicular cells when taking small dose of inorganic iodine in conditions of alimentary iodine deficiency.

We believe that a large number of nodal dots, through which the largest number of correlation connections in the correlation portrait pass (dots with the largest connected content – “main nodal dots”), may indicate a certain instability of the entire system. The presence of nodal dots, through which a small number of correlation connections pass (“additional nodal dots”), can be a sign of significant reserve capabilities of the producer cells of the hormonal product. When the correlation connections in the portrait pass through the nodal dot, their mutual potentiation or mutual weakening is possible, while the effect is directly proportional to the number of connections. In this case, the interaction between correlation connections at the nodal dots has a stabilizing and adapting effect on
the studied direction of cell activity, which turns the nodal dots into important elements of information about regulatory mechanisms. The study of the nodal dots’ nomenclature in the correlation portraits shows the multivariate fields of activity, stabilization, and adaptation of the cell, which indicates that the follicular cell as a hormone producer is a cybernetic self-regulating system.

Since the activity of all its elements in one biological object is interconnected, there is a need to investigate the interdependencies between the organelles of different activity clusters of the “hormone-producing cell” system (in our case, the “follicular cell”) and to find out the significance of the consequences of their mutual influences. In this case, we propose to start the analysis with the definition of the most sensitive to the influences key elements of the studied cluster (organelles), which make up the “feedback system”, “action system” and “attraction system” [42, 43]. The set of cell organelles (and other cellular components) of any cluster, which are the first to react to changes in homeostasis, should be labeled as the “attraction system”. Part of the organelles of the follicular cell, in which changes in homeostasis induce corresponding specific changes, will be called the “feedback system”, and the carrier of influence is called the “action system” (Fig. 4).

![Fig. 4. Generalized scheme of the Conceptual apparatus for the intra- and intersystem research of the capacity profiles of hormone-producing cells.](image)

In the “action system” influence implementers are defined, which are called “action object” and “action dot”. Instead, a “feedback system” defines the structures that have undergone changes (those that respond to the influence): these are called the “feedback object” and the “feedback dot”. The “attraction system” defines those elements that are most sensitive to influence under the studied conditions: they are called “attraction object” and “attraction dot”. Then the interaction between the “action dot”, “feedback dot” and “attraction dot” becomes the basis for creating an in-depth intra-system or inter-system correlation portrait, which can become an integrative model of the studied biological system’s activity and the basis for an expert system. Depending on the research tasks, the content of the entire array of elements that make up the “action system”, “feedback system”, “attraction system”, as well as, accordingly, their “objects” and “dots” may undergo changes.

**Conclusion.** Mathematical generalizations expressed by the means of mathematical language objectify the data obtained during the study, and mathematical analysis carried out within the limits of one biological object or several biological objects helps to trace the dependence of some processes and phenomena on others, which subsequently permits formulating hypotheses regarding the interdependence of various systems functioning in a complete living body. The use of mathematical methods in the analysis of information about the peculiarities in the functioning of biological systems in normal and pathological conditions permits to identify the main and intermediate stages of their
activity, to explain the regularities of the activity of both individual elements of biological systems, as well as their interconnections and interactions in a complete system, to predict the consequences of the course of various processes, to expand the possibilities of intervention to correct pathological changes. Mathematical approaches to the study of biological objects can be quite diverse. The use of a significant arsenal of special means of analysis permits to fairly objectively establish the regularities and peculiarities of the biological systems’ activity in various functional states. The application of author’s Method the semi-quantitative analysis of electronograms, Method for determining the profiles of hormonopoietic cells’ special capacities and Conceptual apparatus for mathematical research of the obtained data has significant diagnostic prospects for a number of disciplines: normal and pathological physiology, histology and pathological morphology, experimental and clinical endocrinology, hygiene, etc., as it permits to establish the specific link of the hormone-producing cell’s special activity in which the disturbance occurred, and to assess the degree of its manifestations.

**Acknowledgements.** The author expresses sincere gratitude to PhD in Physics & Mathematics, Associate Professor Ivanna Dronyuk for relevant remarks during in the preparation of this article.

**Conflict of interest.** The author has approved the article for publication and declare that the research was conducted in the absence of any conflict or potential conflict of interest.

**Funding.** The author state, that this research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

**References.**


