REVIEWS

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ELECTRONIC INFORMATION SYSTEMS IN BIOTECHNOLOGY

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The aim of the work was to generalize and analyze the use of electronic information systems in biotechnology in order to create new versions of these systems. The publications concerning the systems of different types for solving the problems in biotechnology were studied. Similar systems which traditionally belong to biology and medicine were classified. The prospects of their application for development of more advanced electronic systems were considered.

Key words: bioinformatics, electronic information systems, databases.

The progress of contemporary biotechnology-based production in the world is unprecedented. This happened due to the achievements in areas of molecular studies and modeling, discoveries in the field of pharmacology, studies of disease characteristics, achievements in the clinical aspect of health care and, on other hand, due to the intensive development of information technologies (IT) and computer technologies (CT), mainly on the basis of the databases (DB), which gave the opportunity to work with great volumes of obtained digitized results. The notion "information system" (IS) means any system, that is capable to receive, to process, to memorize, and to transmit the information according to classic definition [1, 2]. In our research, like other authors, we distinguished two types of information systems [1, 2]. So, "information system" may mean: 1 — living systems in nature, we suggest to call them "nIS" (natural information systems), and 2 technical information systems, respectively "tIS" (technical information systems), namely this publication is dedicated to the observation of the latter ones. During the last decade the "hybrid" ISs have been developed also; they unite characteristics of nIS and tIS [1]. Present review about the elaboration of modern electronic information systems (ISs) on the basis of databases (DBs) for biotechnology (and biology in general), we have done after the analysis of more than 370 modern sources (since 2000 year), as well as number of earlier works; in general, relevant publications have been reviewed over the past 35-30 years. Below in this article the results were published of such author's original works and analysis of IS use in biotechnology and linked biological and medical disciplines [1-37]. Some other authors' works with the description of tISs for these spheres are in [38-68].

Below the results of our first classification of modern ISs for the facilitation of future ISs' versions construction were suggested; and these ISs can be used in biotechnology. It should be noted that scientific and technical publications about novel tISs (technical information systems) of ten contain a number of deficiencies. Most of them announced only the development of any tIS and give it superficial characteristic which should announce a novelty. But they omitted numerous technical characteristics of the systems, the principles of their functioning, and etc.; all these complicate the analytical research. Despite of this, we have analyzed the experience of modern ISs constructing, which can be applied for successful works in biotechnology. Today all such tISs are network-based [1, 10, 11, 22, 25, 41, 42, 48, 54, 60-62, 67, 69-94] and linked with DBs [95–127]. Content for these databases was obtained usually from the results of biological and medical observations and experiments [4, 5, 10, 12–14, 17, 22–44, 47-49, 61, 68, 71, 74, 78–81, 85, 86–88, 92, 95–97, 106, 112, 117, 119–151].

Further each of the mentioned tISs we have characterized briefly.

The first works on the development of tIS with databases for biotechnology, other *biological and medical sciences*. The importance of IT developments for all biological branches and, first of all, for biotechnology, has often been highlighted during contemporary international forums with the participation of biologists, managers and IT professionals. One of the first important forums — VLDB 2000 Conference — had happened on June, 2000. VLDB 2000 was dedicated to the prediction of the ways of IT development for the biology and medicine; for the control of situation with biodiversity and ecosystems [1, 10]. It was noted that the study of biodiversity and ecosystems refers to those sciences that can (and must be) fully formalized and informative, despite the fact that the objects of their study are extremely complex. The new branch "Informatics in Biodiversity and Ecosystems" (BDEI – **BREI**) was officially started at this meeting. It was emphasized that the diversity of living organisms in nature is an impressive feature of our reality. As a result of biodiversity existence, the people of the Earth were provided with clean air and water, food, homes, medicine, and etc. Finally, the biodiversity based on the existence of ecosystems gives billions dollars to national economies of different countries, either directly, through the agriculture, forestry, fishing, or as a result of protecting crops, pest control practices, soil restoration, carbon dioxide removal, nitrogen fixation, environment perfection. Obviously, $_{\mathrm{this}}$ was one of the most important areas of vital importance; and it is important in terms of science, education, economics and government control. Therefore. the development of electronic ISs, which would enable to realize the scientific study of the nature at the modern level, educational work and rational economic development of nature with the support of governments, was one of the most important tasks of that time. It was emphasized that for 2000-th year humanity has not had yet sufficiently good IT/CT tools for the solution of such problems. Therefore, it was necessary to invent a new generation of such means, including means of satellite environmental

control and computer processing of obtained biological information. At the same time it was necessary to solve the problem of matching and ordering into the linked DBs the entire volume of biological data of various natures, both obtained by digital and classical means during the centuries. This task was extremely complicated, since in electronic databases in ISs should be ordered the latest digitized data at the level of molecular biology, genetics, biochemistry with its processes and reactions, as well as the data from field observations of species, observations of changes in the environment, data of classical taxonomy (and they should correlate with each other!) At the same time, these data should be in such form, that they can be processed, analyzed and compared jointly. One such IT/CT tool for this period was called the "Super Blue Gene", it was the supercomputer which IBM started to develop on 2000 for the analysis of thousands of protein molecules composition of various species living on the Earth.

Classification of information systems with databases for biology and medicine. Primary there were no specific information systems developed specifically for biotechnology it was economically unjustified. The first developed tISs were accepted from both spheres, either medicine or biology, for all the works in biotechnology. Later some of such tISs were modernized and adapted for biotechnological tasks. Therefore, below we offer the classification of tISs developed for medicine and biology that became the resource of the data and procedures for biotechnological works. Let's observe the examples of various modern ISs with DBs in biology and medicine, information about which was published since 2000. Despite the diversity of such systems (and, accordingly, despite the diversity of publications), it was possible to distinguish certain well-defined types of ISs among them. It should be noted that such classification in the finished form in the scientific and technical literature until 2008 did not exist; it is original and the author made it on the basis of materials of about 166 publications.

Presence of large variety of tISs' versions in modern medicine was due to a good funding of the works related to medicine and health protection in the world. Thus, among the ISs with DBs for medicine one can distinguish (Fig. 1): medical ISs of general purposes, expert systems, electronic systems for working with images, electronic systems for working with medical documents, systems for scientific purposes, library medical systems, electronic educational systems in medicine, electronic medical databases.

To the first positions in this list we placed the systems, information about which was published in the most numerical contemporary scientific and technical sources. For example, the group "Medical ISs of general purposes" included large and complex medical ISs developed for hospitals, medical research centers, etc. They united large numbers of sectors, DBs, electronic libraries and other services, sometimes complex networks with information defense and etc. The developers paved great attention to them, respectively, because of health care and health protection purposes. Such ISs were of the greatest demand of users, often embodied in practice in modern hospitals, laboratories and etc. So, these ISs felt into our section "Medical ISs of general purpose". This can be explained by the practical needs of clinical medicine, which requires the most of such versions.

When viewed the list of ISs classification from the top to the end, the number of publications corresponding to one specified type of the system decreases, and in the section "Electronic medical databases" felt to the lowest number of publications. This does not mean that electronic medical DBs were not important in medical practice. Such pattern could also be explained by the fact that the procedure for creating of such databases is standard, described in university textbooks, and perhaps the developers of such DBs did not see them as novelty, required for scientific publications.

Describing the classification of electronic ISs in biological sciences, it was necessary to tell that such ISs types can also be successfully applied in biotechnology. Placing these ISs types in hierarchy (Fig. 2), we followed the same principle as above: the more publications $contain\,modern\,scientific\,and\,technical\,sources$ about this type of systems; respectively, the higher its name was in our list. Similar types of systems in biology and medicine we marked with the same hatch (for example, "Electronic systems for working with images" are marked by a square hatch for all branches; Fig. 1, 2). Regarding to the classification of ISs in biology, most of them were scientific ISs with DBs according to their purposes and the developers paid the main attention to them. Such situation looked like similar to "Medical ISs of general purpose" from Fig. 1. At the same time, such scientific systems in biology also performed educational functions, so, they are (and may be called) "Educational ISs". Further, according to the attention of developers, and consequently, according to the number of developed systems were electronic libraries in biology and biological databases. There were relatively not numerical publications about the systems designed for the work with images. Abovementioned could not be applied to systems for the work with images in anatomy, cytology — such systems were numerous, quite thoroughly developed, because they support some medical operations (for example, surgeons) and computer diagnostics are based on them also. But in our classification, they were at the third position from the top in the

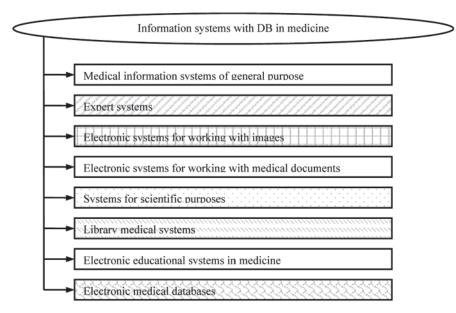


Fig. 1. Information systems with databases for medicine that could be applied in biotechnology [1]

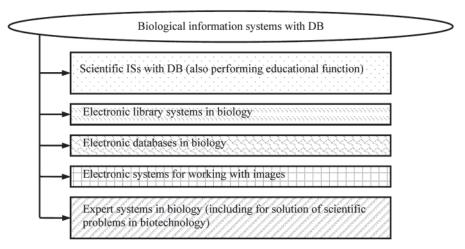


Fig. 2. Biological information systems with databases that could be applied in biotechnology [1]

classification of ISs for medicine, because they are necessary for the needs of this sphere; so, they were first developed and applied with equal intensity in medicine and in biology. Computer expert biological systems were the most close to the biotechnological practice, for example, for the estimation of pests' presence on fields, for bee diseases identification, and etc. Thus, the classification of ISs for biology could be presented as: scientific ISs with DBs (also performing educational function), electronic library systems in biology, electronic databases in biology, electronic systems for the work with images, expert systems in biology (including ones for solution of scientific problems in biotechnology) (Fig. 2).

Information systems with databases in biotechnology and some related biological sciences. Let's observe the examples of ISs with databases in the fields of biology, such as: 1 biotechnology, and namely, those areas where data were used to study the genome, molecular biology and pathophysiology, 2 — related branches of biology, in which biotechnological works are also represented: biodiversity, ecology, adaptive biology. Our attention to the designed electronic ISs in these spheres was due to the fact that the author has her own researches in them during long years.

Technical information systems (tISs) in biotechnology, molecular biology, pathophysiology, genome studies. Some time ago, the achievements in these areas of biology were limited by enough low level of individual genes and biological molecules studies, but accelerated development of computer and ISs for biotechnology made it possible to solve such important tasks as, for example, computer scans of thousands samples per day, high-resolution detection systems (thousands of data points, for example) and the creation of appropriate electronic ISs. In the United States, the National Center for Biotechnology Information (NCBI) has a collection of databases with genetic sequencing data, decoded protein structures, and other biologic information that are updated constantly, and expanding exponentially.

NCBI published the 146th issue of GenBank, this is a publication on the gene sequences database, which contains an information on 42, 734, 478 gene sequences (February 15, 2005). Before there the results of the full decoding of human genome were published (February, 2001). These events had demonstrated two the most prominent achievements in these areas over the previous 10 years. An outstanding feature was that a large set of biological data has been constantly and completely digitized and recorded into the memory of computer domains of electronic ISs for the first time in the world scientific practice, which became an influential factor of the progress in this field. Today, in addition to human genome, there was continuous work on decoding the genomes of many other living organisms, such as mammals, agricultural, viral and bacterial organisms, which gives humanity fundamental knowledge about the information basis of living systems. Another fundamental discovery of modern biotechnology had become the "high-capacity" scan of genome, in which the integrativity (polymorphism of a separate nucleotide) and the activity (gene expression profiling) for each gene in the same genome can be recorded from the same sample.

This was done by using a technology of DNA milieu platform that can detect tens of thousands of genes, using a small functional system like a post stamp, with data immediately recorded into computer's memory. Information coming from the laboratories working with DNA milieu platforms contained thousands of gene-specific measurements per day. So, the general result of the work with the use of such revolutionary technologies also depended on the level of used integrated ISs for the analysis and recording of the data, as well as from the computer system for this gene-specific detection (hybridization).

In the United States, the Food and Drug Administration (FDA) has published guidelines for the development of biotechnological methods, including such as DNA milieu technology platforms, for their use in genetic prognostication and diagnosis of humans; there were indicated that such methods actually initiated a revolution in medicine, which became "more personalized" with their use.

Progress in biochemistry and genome studies faced new challenges, stimulated the development of other branches of science, interdisciplinary research. For example, in [1, 100] it was demonstrated that as a result of the necessity of processing of a huge amounts of experimental data obtained using modern automated experiments in biochemistry, molecular biology, there was a need to create a new set of computer methods and optimization techniques. The peculiarity of such situation was that many of the important problems arising from the researches in computer biochemistry and gene analysis could be formulated in terms of certain combinatorial optimization problems in specially constructed graphs. The authors of the article developed such approaches and offered them to solve new biological problems. The methods used in bioinformatics have been called "the use of mathematical, statistical and computer tools for analyzing of biological data". These were sorting of sequences, phylogenetic trees, predictions of structures, and various modeling methods. Later the recognition was added to this set. Speaking about the main fields of application of computer methods in modern gene and molecular biology, ones told about the study of DNA chains sequences formation, collection of these chains, mapping of genomes, comparison of sequences and analysis of phylogenetic relationships.

The natural extension of IT/CT application in the study of genome and molecular biology phenomena became the field of study and correction of metabolic disorders with IT use [1, 101, 102, 107]. The study of metabolic disorders was focused on the research of metabolic mechanisms, the search for effective

treatment methods, and improvement of clinical diagnosis during the XX century. The successes that have been achieved in deciphering of gene sequences and associated metabolic data, the success in the development of ISs based on the databases of genome and molecular biology research results, elaboration of database on protein and other biomolecules important in terms of metabolism, allowed ones to transfer some of the developed computer methods to the field of study of metabolism and its disorders. In this article the analytical strategies for bioinformatics were used to process current data both at genome level and at level of metabolism, and then the results were combined to explain certain metabolic disorders. For the analysis of biomedical data in disorders the PathAligner Internet Information System was used, and the results were shown on example of urea cycle disorders.

The "Petri net" model was designed to assess the regulation both at the gene level and at the metabolic level. To explain the regulation of the urea cycle, the transcription factors and signaling pathways were also analyzed. It is known that gene/metabolic defects often cause metabolic blockade and lead to the metabolic disorders. In accordance with the current state of development of methods and concepts of bioinformatics for the analysis of metabolic disorders, it was necessary to understand first the ways of reactions that are effected by encoded gene information (directly or indirectly) and to find out how the modification of the reaction phases and the depletion of metabolites reserves affect the overall response of the system of reactions. For the solution of these problems the methods of biomedical information search and system modeling were used. The PathAligner Web-based system was used to allow users to navigate easily in genetic and metabolic related information. The "Petri net" methodology was used to create a model of biomedical system. For example, in the system of urea cycle modeling, a huge volumes of the data from different databases were used; as a result of which the authors described the metabolic paths and mechanisms, regulatory schemes, and etc. Subsequently, the authors wanted to extend these methods to the study of rheumatoid arthritis and other diseases. The design and analysis of signal network allowed the authors to verify the integrity of the data set. The "base network" constructed by the authors was useful for the next simulation, forecasting and comparison of various cellular systems. The obtained

graphical results and the results of dynamic modeling made it possible to understand intuitively the logic of cellular metabolism. Thus, the applied methods of bioinformatics could be considered as non-invasive methods for studying of the functions of genetic and metabolic systems.

The authors of [102] believed that on the basis of their developed methods of bioinformatics, the method for integrating of the data and procedures for the modeling of "Petri net" will be following: 1 — to integrate biological and biomedical data; 2 -to create functional structure models; 3 - to predict genetic predisposition to pathologies, disease detection, improved diagnosis, development of new drugs, toxicology; 4 — to use alternative, compensatory metabolic paths instead of damaged, and etc. As a result, the scientists would be able to use such system analysis, for example, to prevent metabolic disorders and comprehensive testing of drugs before their traditional laboratory testing. The authors considered that their main achievement is to integrate various levels of metabolic data using the existing methods of bioinformatics and computer-based methods on the basis of the databases. They believed that the use of IT/CT can simulate a general scenario of how biomedical systems work, which clinical manifestations can have changes in genes and, consequently, the false changes in the paths of chemical reactions (which follow gene changes); so, what measures are necessary for the prevention of various human pathologies, including oncopathology [110, 111]. Examples of such works using the newly created tISs could be illustrated by Figures 3, 4. Thus, in [110] (Fig. 3), as a result of processing of experimental data from elaborated databases in the corresponding tIS, the authors had found "clusters enriched for genes involved in both cell cycle regulation and cell division, which is biologically reasonable in a cancer orientated dataset". Than they have evaluated their method on both synthetic and gene expression analysis problems.

In other publication [111] (Fig. 4) using the tIS with linked databases with the obtained experimental data, and as a result of automatic processing of these data, the authors wrote that their results provide a novel molecular stratification of the breast cancer population, derived from the impact of somatic copy number aberrations on the transcriptome.

Information systems developed in other spheres of biology, data from which were used in biotechnology: biodiversity, ecology, zoology

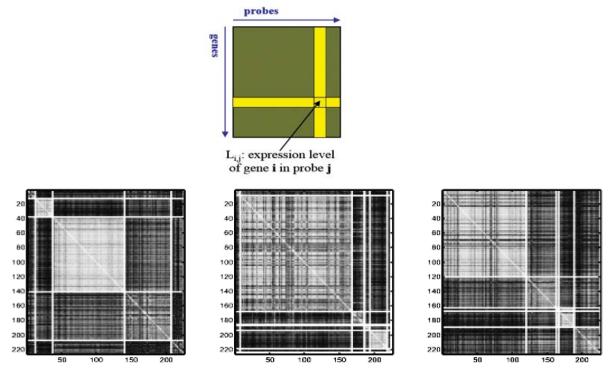


Fig. 3. Clustering of covariance structure (explanations see in text) [110]

Above: The gene expression matrix. L_{I,j}: expression level of gene I in probe j. *Below. Left*: k-means using correlation distance. *Middle*: agglomerating of hierarchical clustering using average linkage and correlation distance. *Right*: DPVC MCMC

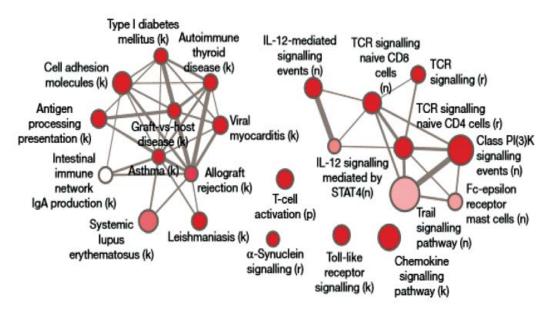


Fig. 4. Trans-acting aberration hotspots modulate concerted molecular pathways (explanations see in text) [111]

[113, 114, 117, 120-122, 134-136, 139-141,146, 147]. In this chapter let's review the experience of elaboration of ISs based on the databases about insects and some other living organisms. The development of such tISs started in the late 1990-th [112]. These systems were named EuroLOOP and BioNET [112]. EuroLOOP was suggested as database about the insects and some other living organisms in Europe. BioNET was developed as similar database system but of a larger scale which, in addition to the databases about European organisms, included collections and data analysis from organisms in some African countries. Later BioNET became a well-known global system. In these two systems developers have acquired the first experience in construction of informational biological systems, taking into account the specifics of biological objects and data. This experience has been used further by ISs' developers in other countries.

Later and more perfect examples of development and use of electronic databases in Internet with a purely academic purpose were following two projects [113, 114]. The "Tree of Life" Web project [114] was a good electronic resource for finding of information, relevant links and hyperlinks on animal and plant diversity (http://tolweb. org). This project satisfied the needs of one who interested in information about the certain groups of organisms. The project was started in early 1980-th by David Maddison and later it was supported by scholars and amateurs throughout the world. The site was structured in the form of a tree with roots, branches and leaves. So-called page-branches were branched off, reflecting the fact that some groups of organisms can be further subdivided into subgroups due to the certain differences in their genotypes. Unlike such groups, phylogenetic groups that formed leaves (and, respectively, in ISs, leaves-pages) corresponding to the terminal groups that are not subdivided into subgroups in nature [114].

If one could go to any page ("branch" or "leaf"), one can find a brief overview of the most important characteristics of a certain group of organisms. In addition, one can access a collection of relevant scientific articles, other accessible Web-resources, notes and comments with additional information and so-called "Treehouses" [114], which were designed for the children as a teaching Webresource. For the most pages the pictures of described organisms — colored illustrations there were presented also.

If the previous databases about the insects were first developed for the Euro-African region, the following two electronic DBs about insect pathogens were visualized in Internet on 1996 [87]. They were developed in the United States and Japan, and they are updated by the material mainly from these regions. For example, in the United States there were already many databases about the different groups of living organisms of this country, such as ANIMAL INFO — Animal Bytes; this was a site for various organisms of animal world, from worms to mammals.

Later the development of IS with living organisms databases started in India, where a technically more complex BODHI system [117] with biodiversity data was elaborated (Fig. 5). The works were conducted under the supervision of Biotechnology Department of the Ministry of Science and Technology with the support of India Government [117]. In electronic databases of this system there should be accumulated the plant world information. The BODHI authors considered as it unique characteristic the possibility to store different types of the data at different levels: from molecular level to organism level. These data also included taxonomic characteristics, geographic distribution, genetic sequences, and others. For the work with these data some specific indexing strategies were developed and used to enable these data access. A special processor was designed to optimize the execution of queries. The BODHI system was an integrative database system, it was an object $oriented \ system \ in \ which \ complex \ objects \ form$ a subordinate hierarchy and sequences that are similar with biodiversity domain in nature.

BODHI was considered to be the first system of nature in which such integrative approach and data aggregation are implemented at different levels of hierarchy systems [117]. The system was based on licensed and accessible

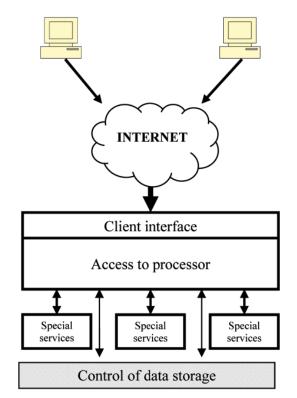


Fig. 5. Scheme of BODHI system architecture (Bedathur) [117]

software and it is provided free of charge. It was implemented on the basis of PC Pentium-III with the operating system Linux. Access to the data in database was carried out on the basis of the structures described in technical literature. For example, the Path-Dictionary and Multi-key Type can accelerate the access in inheritance and aggregation hierarchies, while R* -tree and Hilbert R-tree were used to control spatial queries. BODHI server was compliant with ODMG, it supports OQL/ODL queries, and data modeling interface. In order to permit biologists intuitively easier to work with this system, BODHI also supported access through a Web client-server model, where the client generated its requests through the HTTP protocol and CGI-bin scripts, and results are displayed using the browser interface. And finally, the server was "XML-friendly", the object-results are displayed in XML format, which allows their visualization (Fig. 5) [117].

Developers created BODHI not only as database system by itselves, it plays a more important role. It is also a central repository that provides users with a common platform for information exchange, decision making, packet visualization, and etc. The role of BODHI developers is similar to the role played by the Management Information Base (MIB) system in the management of networks in telecommunications.

Information systems with databases about biological objects developed for the global networks. Contemporary electronic databases with access to the Internet with information about living organisms were the tISs, designed during the last 25 years. They were designed either for academic purposes — to maximize the accumulation of information on groups of living organisms, or for the needs of economy, in particular, for conducting of ecological monitoring, including monitoring of polluted environments. Today all such tISs are networkbased and linked with databases [1, 10, 11, 25, 41, 42, 60–62, 67, 69–71, 90–94, 96–113, 116, 119–126, 133–140, 143–146].

Let's observe several tISs, in which the numerous electronic collections (they are ordered into the databases about the biological organisms) were connected into the one network, uniting segments in different world regions. A number of databases united into such a system should contain information on the types of bioorganisms, their variability, biodiversity, which during monitoring are able to reflect the effect of environmentally harmful influences on these bioorganisms [1, 12, 17, 22, 25, 29, 98–100, 108, 117]. Data from already developed networks with electronic databases demonstrate the high variability of taxonomic groups on a global scale (for example, information from the Global Biodiversity Information Facility), the variability of taxonomic groups in different regions of the Earth (for example, the European Natural History Specimen Information Network) and the variability of areas of the specific taxonomic groups distribution on a planet scale (for example, the Mammal Networked Information System — MANIS) [113]. In frameworks of these projects, the data ordered in disparate electronic databases developed by implementing institutions were linked over the Internet using modern network technologies. In such a way the data of separate and previously disparate electronic collections were actually merged into a single, large-scale centralized collection. So, the user could, in response to one request to receive an information simultaneously from all collections of institutions participated in these projects. These networks contained information about 20-40% of species (approximately 60 million electronic records) up to 2008 [113]. Consequently, since the basic information about numerous species had already been ordered in the electronic database, it was necessary to do the further steps — the addition to biological data the relevant geographic information, standardization, detection of errors and the completion of already developed databases with information about the new species from databases of other networks. The authors considered that fulfillment of these tasks in the context of already developed IS would greatly improve the quality of all ISs in general. Thus, during the creation of the MANIS database, the electronic records from geographic databases were recorded into it, for example, with the information about latitude and longitude, and in process of geographic location determining an error was estimated [113].

Standardization of taxonomic information — the presentation of generally accepted non-conflicting names of species — is another difficulty, if to take into account that information about these species is distributed (and comes to the user) from/to geographically remote compartments of the global network, and such information may differ in databases created in different regions of the world. The work on the collecting and recording of taxonomically correct information about different species is of priority task, since the practical value of the whole project depends on the validity of such information. Consequently, a lot of efforts would be necessary for taxonomic

electronic information correction on a global scale, taking into account also the fact that taxonomy studies are constantly ongoing worldwide, and therefore, such information in electronic databases should be constantly updated and standardized [1, 113].

The similarity of collection contents and observational data in such databases, including Darwin Core (http://speciesanalyst.net/docs/ dwc/) and the group that solve the task of access to biological data collections (Task Group on Access to Biological Collection Data-ABCD; http://www.bgbm.org/TDWG/ CODATA/ Schema/default.htm) [1, 113] allowed ones to search for ordered information and to get it from different data sets. In the framework of some projects, standardization of taxonomic information, which has been distributed in networks, has already been carried out. Such projects included the Integrated Taxonomic (http://www.itis.usda. Information System gov/),Species2000 (http://www.sp2000. org/) and the Electronic Directory of Names of Famous Organisms (Electronic Catalog of Names of Known Organisms - ECAT; http://www.gbif.org/prog/ecat/prog). The databases for these projects were developed close cooperation between taxonomists in and researchers in other fields that provided their data. For data transmission through the Internet within these projects, freely available software was developed by Distributed Generic Information Retrieval (DiGIR; http://digir. sourceforge.net/) for the Darwin Core project and BioCASE Data Transfer Protocol (http:// www.biocase.org/) for the ABCD project. These client-server protocols provided a single source of access to the data received from the few data sources [1].

Information systems with databases, which combine characteristics of both medical and biological ones. In many recent publications it has been demonstrated that development of ISs with databases in medicine and biology is gradually reducing the distance between biological sciences and medicine [1, 120, 132]. This happened due to number of reasons, but mainly because of the fact that many stored data can be used both in clinical practice and in biological research [1]. Besides of this, such branch as biotechnology occupied intermediately positions between these sciences by themselves. Thus, the library system BioMedNet, which contains abstracts of well-known biological and medical journals, is used by biotechnologists, physicians and biologists as well. The same one can say about the library system Academic Press and

Springer, which contain a large number of full-text journals, necessary for biologists and doctors both. To the database with information about proteins and decoded gene sequences apply many professionals — biotechnologists, doctors, specialists from many other biological specialties. In article [120] it was noted that thissituation led to the introduction in the United States, primarily at Columbia University, of new courses in the educational process, which combine biological and medical informatics. After the analysis of the state of the problem, the course "Theory and Methods of Biomedical Informatics" was developed there and approved for studying. A similar course was also studied in the Stanford University. The article [132] outlined the latest for these years' methodologies for the development of ISs with databases. These methodologies were based on ontological principles, the developments of ISs with "mixed" information were used widely; and they combined both the databases with gene information and clinical databases. New ontological methods for development of such ISs were needed to facilitate the information search, access to it, and obtain it from the remote Internet resources. One of the areas of application of new ISs developments are biotechnology and biomedicine. These spheres, on expert opinions, would lead soon to new scientific achievements and would accelerate the works on the program "Human Genome Project". The development of such newest ISs in biotechnology and biomedicine were being conducted by European Commission programs, for example, the INFOGENMED project [1].

Types of information systems that occupied intermediately positions between biology and medicine. As an example of such systems we can observe a neurophysiology; moreover, many professionals in biotechnology are interested in the data obtained in this sphere. Neurophysiology as a branch is at

"intersection" between medical and \mathbf{the} biological sciences. So, some peculiarities of ISs' classification there were similar to both biology and medicine (let's compare figures 1, 2, 6) [1]. Sure, it did not have "Medical ISs of general purpose" group because there is not need in their development — such tasks are important for medical practice only. However, the neurophysiology deals with the solution of purely scientific problems, so developed electronic systems here have to facilitate their solution. There are also the need to develop own large databases and electronic library systems to store numerous experimental neurophysiological results and data from literary sources. So, in the classification list for neurophysiology, some items would coincide with the list for medical ISs, and some with biological ISs. As a result, the general classification for the field of neurophysiology acquired the following form (Fig. 6): expert systems in neurophysiology (including ones for the solution of scientific problems), electronic systems for the work with images, electronic library systems in neurophysiology, and electronic databases in neurophysiology [1].

We could forecast that classification list of ISs types for biotechnology will demonstrate similar regularities as ones for neurophysiology, because this sphere is also at "intersection" between biology and medicine; but final correct conclusions we will be able to make after the upcoming additional studies.

Thus, at the current level of development of computer technologies in the medical and biological practice both older ISs according to time of their development, as well as more recent ideas, methods, technologies and developments coexist successfully [1]. Their role and the attention given to their application are determined by practical activity. The reasons of the fast development of ISs with databases in these spheres are the burst-like

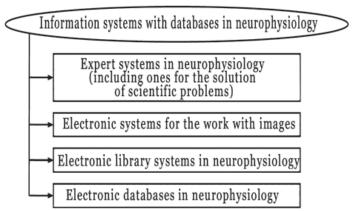


Fig. 6. Information systems with databases in neurophysiology [1]

increase in the amount of input data, which requires the appropriate development of database management systems and ISs.

Medical ISs obtain better funding then biological ones usually, the period of their intensive development was during the last 22–25 years. Consequently, medical ISs demonstrate the greater number of varieties in comparison with biological ones [1]. The first biological ISs were developed on 1980-1990-th, but the period of their intensive development was the last 15–16 years. Among the biological ISs, the first ones are those related to industry (biotechnology), medicine (for physiology, brain biology, etc.) and business (database with information on biological medicinal products, sales sites, and etc.) With regard to such biological ISs, which contain purely academic information, the classification of living organisms, taxonomy data and etc., their examples are not numerical today in comparison with medical ones [1], and their constructing is waiting for their developers still.

Comparing two classifications of modern electronic information systems — in medicine and biology, we can make some conclusions (Fig. 1, 2), basing on publications [1-132].

1. The medical ISs were characterized by the greatest variety and necessity for the practice.

2. Electronic ISs in biology were characterized by the greater proximity to scientific research.

3. Examining the numerous works on the development of various ISs in medicine and biology, we saw that developers are focused on the development of: 1) medical ISs of general purpose; 2) electronic library systems; 3) electronic systems for working with documents; 4) expert systems.

REFERENCES

- 1. Klyuchko O. M. Information and computer technologies in biology and medicine. Kyiv: NAU-druk. 2008, 252 p. (In Ukrainian).
- 2. Piatigorsky B.Ya., Zaitman G.A., Cherkasky V.L., Chinarov V.A. Automatic electrophysiological experiment. Kyiv: Nauk. dumka. 1985. 216 p. (In Russian).
- 3. *Klyuchko O. M.* On the mathematical methods in biology and medicine. *Biotechnol.acta*. 2017, 10(3), 31–40. https://doi.org/10.15407/ biotech10.03.031
- 4. Klyuchko O. M. Application of artificial neural networks method in biotechnology. Biotechnol. acta. 2017, 10(4), 5–13. https:// doi.org/10.15407/biotech10.04.005
- 5. Klyuchko O. M. Cluster analysis in biotechnology. Biotechnol. acta. 2017, 10(5), 5–18. https://doi.org/10.15407/biotech10.05.005

4. In parallel with these types of systems, the following types of ISs were presented in the publications of world scientific and technical literature: 1) electronic systems for working with images; 2) systems for scientific purposes; 3) electronic teaching systems, and etc.

The latter conclusion reflects the fact that the procedure of electronic teaching systems constructing is well developed and does not require special publications, then the elaboration of electronic systems for the work with images and systems for scientific purposes solves often the unique priority tasks, which also results less number of publications with the description of such systems. As example of biological ISs the BODHI system we observed more attentively. It was an integrative database system, an object-oriented system in which complex objects form a subordinate hierarchy and sequences that are similar with biodiversity domains in nature [117].

So, in present publication we generalized and analyzed the experience of electronic information systems with databases use; and such systems may be used for tasks solution in biotechnology. We examined ISs from numerical scientific and technical publications, suitable for the solutions of different tasks in biotechnology. Then we classified such systems, which traditionally refer to both biological and medical sciences. Further we observed different examples of such information systems, as well as systems that have characteristics both medical and biological in order to facilitate the invention of future more advanced electronic information systems for biotechnological purposes.

- 6. Klyuchko O. M. Technologies of brain images processing. Biotechnol. acta. 2017, 10(6), 5–17. https://doi.org/10.15407/biotech10.05.005
- 7. Tasseff R. A. Mathematical Models in Biotechnology. PLoS One, 5:e8864, 2010.
- 8. Mata-Alvarez J. Mathematical Modeling in Biotechnology. Biotechnology. V. II. 2004. https://www.eolss.net/sample-chapters/ C17/ E6-58-02-04.pdf
- 9. Gordeev L. S. Mathematical Modeling in Chemical Engineering and Biotechnology. Theoretical Foundations of Chemical Engineering. 2014, 48 (3), 225–229. https:// link.springer. com/article/10.1134/ S0040579514030099
- 10. Schnase J.L., Cushing J., Frame M. Information technology challenges of biodiversity and ecosystems informatics. Information systems. 2003, 28 (4), 339-345.

- 11. Rana B. K., Insel P. A. G-protein-coupled receptor websites. Trend. Pharmacol. Sci. 2002, 23 (11),535-536. doi: http://dx.doi. org/10.1016/S0165-6147(02)02113-2
- Patent 1370136 USSR, MKH C12N 5/00. The method for dissociation of hippocampal cells. Klyuchko E. M., Tzyndrenko A. Ya. Priority: 31.01.1986; Issued: 30.01.1988, Bull. No 4, 3 p.
- 13. Sigworth F. Single channel registration. Moskva: Mir, 1987. 448 p. (In Russian).
- Kostyuk P. G. Mechanisms of electrical excitability of nerve cells. *Moskva: Nauka*, 1981, 208 p. (In Russian).
- 15. KlyuchkoO.M., PaskivskyA.O., Sheremet D.Y. Computer modeling of some nanoelements for radio and television systems. *Electr. Contr. Syst.* 2012, 3 (33), 102–107. (In Ukrainian).
- Klyuchko O. M., Hayrutdinov R. R. Modeling of electrical signals propagation in neurons and its nanostructures. *Electr. Contr. Syst.* 2011, 2 (28), 120–124. (In Ukrainian).
- Trinus K. F., Klyuchko E. M. Mediators influence on motoneurons retrogradly marked by primulin. *Physiol. J.* 1984. 30 (6), 730-733 (In Russian).
- Aralova N. I., Klyuchko O. M., Mashkin V. I., Mashkina I. V. Algorithmic and program support for optimization of interval hypoxic training modes selection of pilots. *Electr. Contr. Syst.* 2017, 2 (52), 85–93.
- 19. Aralova N. I., Klyuchko O. M., Mashkin V. I., Mashkina I. V. Mathematic and program models for investigation of reliability of operator professional activity in "Human-Machine" systems. *Electr. Contr. Syst.* 2017, 1 (51), 105–113.
- 20. Aralova N. I., Klyuchko O. M., Mashkin V. I., Mashkina I. V. Mathematical model for research of organism restoring for operators of continuously interacted systems. *Electr. Contr.* Syst. 2016, 3 (49), 100–105.
- 21. Aralova N. I., Klyuchko O. M., Mashkin V. I., Mashkina I. V. Investigation of reliability of operators work at fluctuating temperature conditions. *Electr. Contr. Syst.* 2016, 2 (48), 132–139.
- Plakhotnij S. A., Klyuchko O. M., Krotinova M. V. Information support for automatic industrial environment monitoring systems. *Electr. Contr. Syst.* 2016, 1 (47), 19–34.
- 23. OnopchukYu.M., AralovaN.I., KlyuchkoO.M., Beloshitsky P. V. Mathematic models and integral estimation of organism systems reliability in extreme conditions. Electronics and control systems. 2015, 4 (46), 109–115.
- 24. OnopchukYu.M.,AralovaN.I.,KlyuchkoO.M., Beloshitsky P. V. Integral estimations of human reliability and working capacity in sports wrestling. Journal of the Engineering Academy. 2015, V. 3, P. 145-148.

(In Russian).

- 25. KlyuchkoO.M., ShutkoV.N., NavrotskyiD.O., MikolushkoA. M. The set of program models for ecological monitoring technical system based on principles of biophysics. *Electr. Contr. Syst.* 2014, 4 (42), 135–142.
- 26. Klyuchko O. M., Sheremet D. Yu. Computer simulation of biological nanogenerator functions. *Electr. Contr. Syst.* 2014, 2 (40), 103-111.
- 27. Klyuchko O. M., Shutko V. N. Computer modeling of auto-oscillating phenomena in neuron complexes. *Electr. Contr. Syst.* 2014, 1 (39), 127–132.
- Klyuchko O. M., Sheremet D. Yu. Computer modeling of biologic voltage-activated nanostructures. *Electr. Contr. Syst.* 2014, 1 (39), 133–139.
- 29. Beloshitsky P. V., Klyuchko O. M., Onopchuk Yu. M. Radiation damage of organism and its correction in conditions of adaptation to highmountain meteorological factors. Bulletin of NAU. 2010, V.1, P. 224–231. (In Ukrainian).
- 30. Beloshitsky P. V., Klyuchko O. M., Onopchuk Yu., Makarenko M. V. Estimation of psycho-physiological functions of a person and operator work in extreme conditions. Bulletin of NAU. 2009, No 3, P. 96-104. (In Ukrainian).
- BeloshitskyP.V.,KlyuchkoO.M.,OnopchukYu., KolchinskaA.Z. Results of research of higher nervous activity problems by Ukrainian scientists in Prielbrussie. Bulletin of NAU. 2009, No 2, P. 105–112. (In Ukrainian).
- 32. BeloshitskyP.V.,KlyuchkoO.M.,OnopchukYu. Results of research of structural and functional interdependencies by Ukrainian scientists in Prielbrussie. Bulletin of NAU. 2009, No 1, P. 61–67. (In Ukrainian).
- 33. Beloshitsky P. V., Klyuchko O. M., Onopchuk Yu. Results of research of highlands factors influence on health and longevity by Ukrainian scientists in Prielbrussie. Bulletin of NAU. 2008, No 4, P. 108–117. (In Ukrainian).
- 34. Onopchuk Yu. M., Klyuchko O. M., Beloshitsky P. V. Development of mathematical models basing on researches of Ukrainian scientists at Elbrus. Bulletin of NAU. 2008, No 3, P.146-155. (In Ukrainian).
- 35. BeloshitskyP.V.,KlyuchkoO.M.,OnopchukYu. Results of research of adaptation problems by Ukrainian scientists in Prielbrussie. Bulletin of NAU. 2008, No 1, P. 102–108. (In Ukrainian).
- 36. BeloshitskyP.V.,KlyuchkoO.M.,OnopchukYu. Results of research of hypoxia problems by Ukrainian scientists in Elbrus region. Bulletin of NAU. 2007, No 3–4, P. 44–50. (In Ukrainian).

- 37. Beloshitsky P. V., Klyuchko O. M., Onopchuk Yu. Results of medical and biological research of Ukrainian scientists at Elbrus. Bulletin of NAU. 2007, No 2, P. 10–16. (In Ukrainian).
- Belan P. V, Gerasimenko O. V., Tepikin A. V., Petersen O. H. Localization of Ca++ extrusion sites in pancreatic acinar cells. J. Biol. Chem. 1996, V. 271, P. 7615–7619.
- 39. Belan P., Gardner J., Gerasimenko O. Extracellular Ca++ spikes due to secretory events in salivary gland cells. J. Biol. Chem. 1998, V. 273, P. 4106-4111.
- 40. Jabs R., Pivneva T., Huttmann K. Synaptic transmission onto hyppocampal glial cells with hGFAP promoter activity. J. Biol. Chem. 2005, V. 118, P. 3791–3803.
- 41. Gavrilovich M. Spectra image processing and application in biotechnology and pathology. Dissertation for Ph.D. Acta Universitatis Upsaliensis. Upsala. 2011, 63 p.
- 42. Perner P., Salvetti O. Advances in Mass Data Analysis of Images and Signals in Medicine, Biotechnology, Chemistry and Food Industry. Third International Conference, Leipzig, (Germany): Springer, 2008, Proceedings. 2008, 173 p.
- 43. Baert P., Meesen G., De Schynkel S., Poffijn A., Oostveldt P. V. Simultaneous in situ profiling of DNA lesion endpoints based on image cytometry and a single cell database approach. *Micron.* 2005, 36 (4), 321330. https://doi. org/10.1016/j.micron.2005.01.005.
- 44. Berks G., Ghassemi A., von Keyserlingk D. G. Spatial registration of digital brain atlases based on fuzzy set theory. Comp. Med. Imag. Graph. 2001, 25 (1), 1–10. https://doi. org/10.1016/S0895-6111(00)00038-0.
- 45. Nowinski W. L., Belov D. The Cerefy Neuroradiology Atlas: a Talairach-Tournoux atlas-based tool for analysis of neuroimages available over the internet. NeuroImage. 2003, 20(1), 50-57. https:// doi. org/10.1016/S1053-8119(03)00252-0.
- 46. Chaplot S., Patnaik L. M., Jagannathan N. R. Classification of magnetic resonance brain images using wavelets as input to support vector machine and neural network. Biomed. Signal Process. Control. 2006, 1 (1), 86-92. https:// doi.org/10.1016/j. bspc.2006.05.002.
- 47. KovalevV.A., Petrou M., Suckling J. Detection of structural differences between the brains of schizophrenic patients and controls. Psychiatry Research: Neuroimaging. 2003, 124 (3), 177–189. https://doi.org/10.1016/ S0925-4927(03) 00070-2.
- 48. Araújo T. Classification of breast cancer histology images using Convolutional Neural Networks. PloS One. 2017, 12 (6), e0177544.

- 49. Vecht-Lifshitz S.E., Ison A.P. Biotechnological applications of image analysis: present and future prospects. J. Biotechnol. 1992, 23 (1), 1–18.
- 50. Toga A. W., Thompson P. M. The role of image registration in brain mapping. Image Vis. Comput. 2001, 19 (1-2), 3-24.
- 51. Carro S. A., Scharcanski J. A framework for medical visual information exchange on the WEB. Comput. Biol. Med. 2006, V. 4, P. 327-338.
- 52. Chakravarty M. M., Bertrand G., Hodge C. P., Sadikot A. F., Collins D. L. The creation of a brain atlas for image guided neurosurgery using serial histological data. NeuroImage.2006, 30(2), 359– 376. doi: 10.1016/j.neuroimage.2005.09.041.
- 53. Dikshit A., Wu D., Wu C., Zhao W. An online interactive simulation system for medical imaging education. Comp. Med. Imag. Graph. 2005, 29 (6), 395404. https://doi. org/10.1016/j.compmedimag.2005.02.001.
- 54. Singh R., Schwarz N., Taesombut N., Lee D., Jeong B., Renambot L., Lin A. W., West R., OtsukaH., NaitoS., PeltierS.T., MartoneM.E., Nozaki K., Leigh J., EllismanM.H. Realtime multi-scale brain data acquisition, assembly, and analysis using an end-to-end. OptIPuter Fut. Gener. Comp. Syst. 22 (2006), 1032-1039.
- 55. Stefanescu R., Pennec X., Ayache N. Grid powered nonlinear image registration with locally adaptive regularization. Med. Imag. Anal. 2004. 8 (3), 325-342.
- 56. Ma Y., Hof P. R., Grant S. C., Blackband S. J., Bennett R., Slatest L., McGuigan M. D., Benveniste H. A three-dimensional digital atlas database of the adult C57BL/6J mouse brain by magnetic resonance microscopy. Neuroscience. 2005, 135 (4), 12031215. doi: 10.1016/j.neuroscience.2005.07.014.
- 57. Yu-Len Huang. Computer-aided Diagnosis Using Neural Networks and Support Vector Machines for Breast Ultrasonography. J. Med. Ultrasound. 2009,17 (1), 17-24.
- 58. Prachi Damodhar Shahare, Ram Nivas Giri. Comparative Analysis of Artificial Neural Network and Support Vector Machine Classification for Breast Cancer Detection. Int. Res. J. Engineer. Technol. (IRJET). 2015, 2 (9).
- 59. Natrajan R., Sailem H., Mardakheh F. K., Garcia M. F., Tape C. G., Dowsett M., Bakal C., Yuan Y. Microenvironmental heterogeneity parallels breast cancer progression: a histology-genomic integration analysis. *PLoS medicine*. 2016, 13(2), e1001961. https:// doi.org/10.1371/journal.pmed.1001961.
- 60. Klyuchko O. M. Brain images in information systems for neurosurgery and neurophysiology. *Electr. Contr. Syst.* 2009, 3(21), 152–156. (In Ukrainian).

- 61. Klyuchko O. M. Using of images' databases for diagnostics of pathological changes in organism tissues. *Electronics and control* systems. 2009, 2 (20), 62–68. (In Ukrainian).
- 62. Klyuchko O. M. Elements of different level organization of the brain as material for electronic databases with images. *Electronics* and control systems. 2009, 1 (19), 69-75. (In Ukrainian).
- 63. Steimann F. On the representation of roles in object-oriented and conceptual modelling. Data& Knowedge Engineering. 2000, 35 (1), 83-106.
- 64. Klyuchko O. M., Managadze Yu. L., Pashkivsky A. O. Program models of 2D neuronal matrix for ecological monitoring and images' coding. Bulletin of the Engineering Academy. 2013, No 3–4, P. 77–82. (In Ukrainian).
- 65. KlyuchkoO.M., PiatchaninaT.V., MazurM.G. Combined use of relation databases of images for diagnostics, therapy and prognosis of oncology diseases. "Integrated robototechnic complexes". X IIRTC-2017 Conference Proceedings. P. 275–276. (In Ukrainian).
- 66. Shutko V. M, Shutko O. M., Kolganova O. O. Methods and means of compression of information. Kyiv: Nauk. dumka. 2012. 168 p. (In Ukrainian).
- 67. Jecheva V., Nikolova E. Some clusteringbased methodology applications to anomaly intrusion detection systems. Int. J. Secur. Appl. 2016, 10 (1), 215–228. http://dx.doi. org/10.14257/ijsia.2016.10.1.20.
- Iakovidis D. K., Maroulis D. E., Karkanis S.A. Texture multichannel measurements for cancer precursors' identification using support vector machines. *Measurement*. 2004, V. 36, P. 297-313. 2004.09.010 https://doi.org/10.1016/j.measurement.
- NguyenH.Q., Carrieri-KohlmanV., RankinS.H., Slaughter R, Stulbarg M. S. Internet-based patient education and support interventions: a review of evaluation studies and directions for future research. Comp. Biol. Med. 2004, 34 (2), 95–112. doi: 10.1016/S0010-4825(03)00046-5.
- 70. Jézéquel P., Loussouarn L., Guérin-Charbonnel C., Campion L., Vanier A., Gouraud W., Lasla H., Guette C., Valo I., Verrièle V. Campone M. Gene-expression molecular subtyping of triple-negative breast cancer tumours: importance of immune response. Breast Cancer Res. 2015, 17 (1), 43. https:// doi.org/10.1186/s13058-015-0550-y.
- 71. Bozhenko V. K. Multivariable analysis of laboratory blood parameters for obtaining diagnostic information in experimental and clinical oncology. The dissertation author's abstract on scientific degree editions. Dc. Med. Study. Moscow. 2004. (In Russian).
- 72. Ko J. H., Ko E. A., Gu W., Lim I., Bang H., Zhou T. Expression profiling of ion channel

genes predicts clinical outcome in breast cancer. *Mol. Cancer.* 2013, 12 (1), 106. doi: 10.1186/1476-4598-12-106.

- 73. Kawai M., Nakashima A., Kamada S., Kikkawa U. Midostaurin preferentially attenuates proliferation of triple-negative breast cancer cell lines through inhibition of Aurora kinase family. J. Biomed. Sci. 2015, 22 (1), 48. doi: 10.1186/s12929-015-0150-2.
- 74. Uhr K., Wendy J. C., Prager-van der Smissen, Anouk A. J. Heine, Bahar Ozturk, Marcel Smid, Hinrich W. H. G hlmann, Agnes Jager, John A. Foekens, John W. M. Martens. Understanding drugs in breast cancer through drug sensitivity screening. SpringerPlus. 2015, 4(1), 611. doi: 10.1186/ s40064-015-1406-8.
- 75. Onopchuk Yu. M., Biloshitsky P. V., Klyuchko O. M. Development of mathematical models based on the results of researches of Ukrainian scientists at Elbrus. Bulletin of NAU. 2008, No 3, P. 146-155. (In Ukrainian).
- 76. Ankur Poudel, Dhruba Bahadur Thapa, Manoj Sapkota. Cluster Analysis of Wheat (Triticum aestivum L.) Genotypes Based Upon Response to Terminal Heat Stress. Int. J. Appl. Sci. Biotechnol. 2017, 5 (2), 188– 193. doi: http://dx.doi.org/10.3126/ijasbt. v5i2.17614.
- 77. Zaslavsky L., Ciufo S., Fedorov B., Tatusova T. Clustering analysis of proteins from microbial genomes at multiple levels of resolution. BMC Bioinform. 2016, 17 (8), 276. Published online 2016 Aug 31. doi: 10.1186/s12859-016-1112-8.
- Zhou J., Richardson A.J., Rudd K. E. EcoGene-RefSeq: EcoGene tools applied to the RefSeq prokaryotic genomes. *Bioinformatics*. 2013, 29 (15), 1917–1918. Published: 04 June 2013. doi: 10.1093/bioinformatics/btt302.
- 79. Zhang J., Wu G., Hu X., Li S., Hao S. A Parallel Clustering Algorithm with MPI — MKmeans. J. Comput. 2013, 8 (1), 1017. doi: 10.1109/ PAAP. 2011.17.
- 80. Tatusova T., Zaslavsky L., Fedorov B., Haddad D., Vatsan A., Ako-adjei D., Blinkova O., Ghazal H. Protein Clusters. The NCBI Handbook [Internet]. 2nd edition. Available at https:// www.ncbi.nlm.nih.gov/books/ NBK242632.
- 81. Anderson J.G. Evaluation in health informatics: computer simulation. Comp. Biol. Med. 2002, 32 (3), 151–164. https:// doi.org/10.1016/ S0010-4825(02)00012-4.
- 82. Aruna P., Puviarasan N., Palaniappan B. An investigation of neuro-fuzzy systems in psychosomatic disorders. *Exp. Syst.* Appl. 2005, 28 (4), 673–679. https://doi. org/10.1016/j. eswa.2004.12.024.
- 83. Bange M. P., Deutscher S. A., Larsen D., Linsley D., Whiteside S. A handheld decision

support system to facilitate improved insect pest management in Australian cotton systems. *Comp. Electron. Agricult.* 2004, 43 (2), 131–147. https:// doi.org/10.1016/j. compag.2003.12.003.

- 84. Beaulieu A. From brainbank to database: the informational turn in the study of the brain. Stud. Hist. Phil. Biol. Biomed. Sci. 2004, V. 35, P. 367–390. https://doi.org/10.1016/j. shpsc.2004.03.011.
- 85. Horn W. AI in medicine on its way from knowledge-intensive to data-intensive systems. Artif. Intell Med. Elsevier. 2001, 23 (1), 512. https://doi.org/10.1016/S0933-3657(01)00072-0.
- 86. Brake I. Unifying revisionary taxonomy: insect exemplar groups. Abstr. XV SEL Congr. Berlin (Germany). 2007.
- 87. Braxton S. M., Onstad D. W., Dockter D. E., Giordano R., Larsson R., Humber R. A. Description and analysis of two internet-based databases of insect pathogens: EDWIP and VIDIL. J. Invertebr. Pathol. 2003, 83 (3), 185– 195. doi: 10.1016/S0022-2011(03)00089-2.
- 88. BreauxA.,CochraneS.,EvensJ.,MartindaledM., Pavlike B., Suera L., Benner D. Wetland ecological and compliance assessments in the San Francisco Bay Region, California, USA. J. Environm. Manag. 2005, 74 (3), 217–237.
- 89. Budura A., Cudré-Mauroux P., Aberer K. From bioinformatic web portals to semantically integrated Data Grid networks. Fut. Gener. Comp. Syst. 2007, 23 (3), 281-522. doi: 10.1016/j.jenvman. 2004.08.017.
- 90. Burns G., Stephan K. E., Ludäscher B., Gupta A., Kötter R. Towards a federated neuroscientific knowledge management system using brain atlases. Neurocomputing. 2001, V. 3840, P. 1633-1641. https://doi. org/10.1016/S0925-2312(01)00520-3.
- 91. Butenko S., Wilhelm W. E. Clique-detection models in computational biochemistry and genomics. Eur. J. Oper. Res. 2006, 173 (1), 117. https://doi.org/ 10.1016/j. ejor.2005.05.026.
- 92. Carro S. A., Scharcanski J. Framework for medical visual information exchange on the WEB.Comp.Biol.Med.2006,36(4),327–338. doi: 10.1016/j.compbiomed.2004.10.004.
- 93. Chau M., Huang Z., Qin J., Zhou Y., Chen H. Building a scientific knowledge web portal: The NanoPort experience. Decis. Support Syst. 2006. https://doi.org/10.1016/j. dss.2006.01.004.
- 94. Chen M., Hofestädt R. A medical bioinformatics approach for metabolic disorders: Biomedical data prediction, modeling, and systematic analysis. J. Biomed. Inform. 2006, 39 (2), 147–159. https://doi.org/10.1016/j. jbi.2005.05.005.

- 95. Chli M., De Wilde P. Internet search: Subdivision-based interactive query expansion and the soft semantic web. Appl. Soft Comp. 2006. https://doi.org/10.1016/j. asoc.2005.11.003.
- 96. Despont-Gros C., Mueller H., Lovis C. Evaluating user interactions with clinical information systems: A model based on human- computer interaction models. J. Biomed. Inform. 2005, 38 (3), 244-255. https://doi.org/10.1016/j.jbi.2004.12.004.
- 97. Marios D., Dikaiakos M. D. Intermediary infrastructures for the World Wide Web. Comp. Networks. 2004, V. 45, P. 421-447. https:// doi.org/ 10.1016/j. comnet.2004.02.008.
- 98. Dimitrov S. D., Mekenyan O. G, Sinks G. D., Schultz T. W. Global modeling of narcotic chemicals: ciliate and fish toxicity. J. Mol. Struc.: Theochem. 2003, 622 (12), 63–70. https://doi. org/10.1016/S0166-1280(02)00618-8.
- 99. Dong Y., Zhuang Y., Chen K., Tai X. A hierarchical clustering algorithm based on fuzzy graph connectedness. Fuzzy Sets. Syst. 2006, V. 157, P. 1760–1774. https:// doi. org/10.1016/j.fss.2006.01.001.
- 100. Duan Y., Edwards J.S., Xu M.X. Web-based expert systems: benefits and challenges. Inf. Manag. 2005, 42 (6), 799811. https:// doi.org/10.1016/j.im.2004. 08.005.
- 101. Essen van D. C. Windows on the brain: the emerging role of atlases and databases in neuroscience. Curr. Opin. Neurobiol. 2002, 12 (5), 574-579. https://doi.org/10.1016/ S0959-4388(02)00361-6.
- 102. Fellbaum C., Hahn U., Smith B. Towards new information resources for public health From Word Net to Medical Word Net. J. Biomed. Inform. 2006, 39 (3), 321-332. doi: 10.1016/j.jbi.2005.09.004.
- 103. Ferraris M., Frixione P., Squarcia S. Network oriented radiological and medical archive. Comp. Physics Commun. 2001, V. 140, P. 226-232. https://doi.org/10.1016/ S0010-4655(01)00273-9.
- 104. Flower D. R., Attwood T. K. Integrative bioinformatics for functional genome annotation: trawling for G protein-coupled receptors. Reviews 55 Semin. Cell. Dev. Biol. 2004, 15 (6), 693-701. doi: 10.1016/j. semcdb.2004.09.008.
- 105. Fink E., Kokku P. K., Nikiforou S., Hall L. O., Goldgof D. B., Krischer J. P. Selection of patients for clinical trials: an interactive webbased system. Art. Intell. Med. 2004, 31(3), 241–254. doi: 10.1016/j.artmed.2004.01.017.
- 106. Fitzpatrick M.J., Ben-Shahar Y., Smid H.M., Vet L. E., Robinson G. E., Sokolowski M. B. Candidate genes for behavioural ecology. Trend Ecol. Evol. 2005, 20 (2), 96–104. doi: 10.1016/j.tree.2004.11.017.

- 107. FoxJ., AlabassiA., PatkarV., RoseT., BlackE. An ontological approach to modelling tasks and goals. Comp. Biol. Med. 2006, V. 36, P. 837–856. https://doi.org/10.1016/j. compbiomed.2005.04.011.
- 108. Fu Zetian, Xu Feng, Zhou Yun, Shuan X. Z. Pig-vet: a web-based expert system for pig disease diagnosis. Fuzzy Sets. Syst. 2006. https://doi.org/10.1016/j.eswa.2005.01.011.
- 109. Gaulton A., Attwood T. K. Bioinformatics approaches for the classification of G-protein-coupled receptors. Curr. Opin. Pharmacol. 2003, 3 (2), 114–120. doi: 10.1016/S1471-4892(03)00005-5.
- 110. Palla K., Ghahramani Z., Knowles D. A. A nonparametric variable clustering model. Adv. Neural. Inform. Proc. Syst. 2012, 2987–2995.
- 111. Curtis C. L., Shah S. P., Chin S. F., Turashvili G., Rueda O. M., Dunning M. J., Speed D., Lynch A. G., Samarajiwa S., Yuan Y., Gräf S., Ha G., Haffari G., Bashashati A., Russell R., McKinney S.; METABRIC Group, Langerød A., Green A., Provenzano E., Wishart G., Pinder S., Watson P., Markowetz F., Murphy L., Ellis I., Purushotham A., Børresen-Dale A. L., Brenton J. D., Tavaré S., Caldas C., Aparicio S. The genomic and transcriptomic architecture of 2,000 breast tumours reveals novel subgroups. Nature. 2012, 486 (7403), 346–352.
- 112. Proceedings of the second EuroLOOP Workshop, Amsterdam, 27–30 March 1995.
- 113. Graham C. H., Ferrier S., Huettman F., Moritz C., Peterson A. T. New developments in museum-based informatics and applications in biodiversity analysis. Trend. Ecol. Evol. 2004, 19 (9), 497–503. https:// doi. org/10.1016/j.tree.2004.07.006.
- 114. Anokhin B., Hemmrich G. Zoology www guide. Zoology. V. 108, Is. 4, 2005, P. 673-679.
- 115. Hirano S., Sun X., Tsumoto S. Comparison of clustering methods for clinical databases. Inform. Sci. 2004, 159 (34), 155–165. https:// doi.org/ 10.1016/j. ins.2003.03.011.
- 116. Hong Yu., Hatzivassiloglou V., Rzhetsky A., Wilbur W. J. Automatically identifying gene/protein terms in MEDLINE abstracts. J. Biomed. Inform. 2002, 35 (56), 322– 330. https://doi. org/10.1016/S1532-0464(03)00032-7.
- 117. Bedathur S. J., Haritsa J. R., Sen U. S. The building of BODHI, a bio-diversity database system. Inform. Syst. 2003, 28 (4), 347367. https://doi.org/ 10.1016/S0306-4379(02)00073-X.
- 118. *Hsi-Chieh Lee*, *Szu-Wei Huang*, *Li E. Y.* Mining protein-protein interaction information on the internet. *Exp. Syst. Appl.*

Elsevier. 2006, 30 (1), 142–148. https://doi.org/10.1016/j.eswa.2005.09.083.

- 119. Young R.Genetic toxicology: web-resources. Toxicology. 2002, 173 (1-2), P. 103-121.
- 120. Johnson S. B., Friedman R. Bridging the gap between biological and clinical informatics in a graduate training program. J. Biomed. Inform. 2007, 40 (1), 59–66. Epub. 2006 Mar 15. doi: 10.1016/j.jbi.2006.02.011.
- 121. *KaiserM.,HilgetagC.C.* Modelling the development of cortical systems networks. *Neurocomputing*. 2004, V. 5860, P. 297–302. https://doi.org/10.1016/j.neucom.2004.01.059.
- 122. Kane M. D., Brewer J. L. An information technology emphasis in biomedical informatics education. J. Biomed. Inform. 2007, 40 (1), 67–72. https://doi. org/10.1016/j.jbi.2006.02.006.
- 123. Kannathal N., Acharya U. R., Lim C. M., Sadasivan P. K. Characterization of EEG. A comparative study. Comp. Meth. Progr. Biomed. 2005, 80 (1), 17–23. https://doi. org/10.1016/j.cmpb.2005.06.005.
- 124. Koh W., McCormick B. H. Brain microstructure database system: an exoskeleton to 3D reconstruction and modelling. Neurocomputing. 2002, V. 4446, P. 1099-1105. https:// doi.org/10.1016/ S0925-2312(02)00426-5.
- 125. Koh W., McCormick B. H. Registration of a 3D mouse brain atlas with brain microstructure data. Neurocomputing. 2003, V. 5254, P. 307-312. https://doi. org/10.1016/S0925-2312(02)00793-2.
- 126. KulishV., SourinA., SourinaO. Humanelectro encephalograms seen as fractal time series: Mathematical analysis and visualization. Comp. Biol. Med. 2006, 36 (3), 291–302. doi: 10.1016/j.compbiomed.2004.12.003.
- 127. Lubitz von D., Wickramasinghe N. Networkcentric healthcare and bioinformatics: Unified operations within three domains of knowledge. Exp. Syst. Appl. 2006, 30 (1), 11–23. https://doi. org/10.1016/j. eswa.2005.09.069.
- 128. Martin-Sanchez F., Iakovidis I., Norager S., MaojoV., de Groen P., Van der Lei J., Jones T., Abraham-Fuchs K., Apweiler R., Babic A., Baud R., Breton V., Cinquin P., Doupi P., Dugas M., Eils R., Engelbrecht R., Ghazal P., Jehenson P., Kulikowski C., Lampe K., De Moor G., Orphanoudakis S., Rossing N., Sarachan B., Sousa A., Spekowius G., Thireos G., Zahlmann G., Zvárová J., Hermosilla I., Vicente F. J. Synergy between medical informatics and bioinformatics: facilitating genomic medicine for future health care. J. Biomed. Inform. 2004, 37 (1), 30–42. doi:10.1016/j.jbi.2003.09.003.
- 129. Masseroli M., Visconti A., Bano S. G. Pinciroli F. He@lthCo-op: a web-based

system to support distributed healthcare co-operative work. *Comp. Biol. Med.* 2006, 36 (2), 109–127. doi:10.1016/j. compbiomed.2004.09.005.

- 130. Moon S., Byun Y., Han K. FSDB: A frameshift signal database. Comp. Biol. Chem. 2007, 31 (4), 298-302. doi: 10.1016/j.compbiolchem.2007.05.004.
- 131. Orgun B., Vu J. HL7 ontology and mobile agents for interoperability in heterogeneous medical information systems. Comp. Biol. Med. 2006, 36 (78), 817–836. https://doi. org/10.1016/j.compbiomed.2005.04.010.
- 132. Pérez-Rey D., Maojo V., García-Remesal M., Alonso-Calvo R., Billhardt H., Martin-Sánchez F., Sousa A. Ontofusion: Ontology-based integration of genomic and clinical databases. Comp. Biol. Med. 2006, 36 (78), 712-730. doi: 10.1016/j. compbiomed.2005.02.004.
- 133. KrishtalO.A., Kiskin N.I., TsyndrenkoA.Ya., Klyuchko E. M. Pharmacological properties of amino acid receptors in isolated hippocampal neurons. In: Receptors and ion channels. Ed. By Ovchinnikov Y.A., Hucho F. Berlin-New York: Walter de Gruyter, 1987, P. 127–137.
- 134. Klyuchko E. M., Klyuchko Z. F., Beloshitsky P. V. Some adaptation characteristics of insects in mountains of Prielbrussie. Nalchik (Russia), "Hypoxia: automatic analysis of hypoxic states of healthy people and sick ones". 2005, V. 1, P. 137–140. (In Russian).
- 135. Klyuchko Z. F., Klyuchko E. M. Analysis of taxonomic structure of moth fauna (Lepidoptera: Noctuidae s.l.) of Ukraine according to monitoring data. Eversmannia. 2012, 3 (33), 41-45. (In Russian).
- 136. Klyuchko Z. F., Klyuchko E. M. Moth (Lepidoptera: Noctuidae s. l.) of Chercasska region of Ukraine according to results of many-year monitoring. Eversmannia. 2014, No 37, 32-49. (In Russian).
- 137. Gonchar O., Klyuchko O., Seredenko M., Oliynyk B. Correction of metabolic disorders at hypoxia by new pharmacological preparations. Mater. 3 FEPS Congress. Nice (France), 2003, P. 228.
- 138. Seredenko M., Gonchar O., Klyuchko O., Oliynyk S. Peculiarities of prooxidant antioxidant balance of organism under hypoxia of different genesis and its corrections by new pharmacological preparations. Acta Physiologica Hungarica. Budapest (Hungary). 2002, 89 (1-3), 292.
- 139. Klyuchko O., Klyuchko Z., Lizunova A. Electronic Noctuidae database: some problems and solutions. Proceed. 16th European Congress of Lepidopterology. Cluj (Romania), 2009, P. 31-32.

- 140. Klyuchko O., Klyuchko Z., Lizunova A. Noctuidae fauna of Ukrainian Karpathy: results of monitoring (1956–2008). Proceed. 16th European Congress of Lepidopterology. Cluj (Romania), 2009. P. 31.
- 141. Klyuchko O. M., Beloshitsky P. V. Investigation of insect adaptation characteristics in Prielbrussie in 2004–2005. Mater. VIII World Congress of International Society for Adaptive Medicine (ISAM). Moskva (Russia). 2006, P. 165–166.
- 142. Beloshitsky P. V., Klyuchko O. M. Contribution of Sirotinin's school into adaptation medicine. Mater. VIII World Congress of International Society for Adaptive Medicine (ISAM). Moskva (Russia), 2006. P. 158.
- 143. Klyuchko O. M., Klyuchko Z. F. Ukrainian Noctuidae Database. Mater. XIV SEL Congress. Roma (Italy), 2005, P. 49.
- 144. Klyuchko Z. F., Klyuchko O. M. Noctuidae (Lepidoptera) of Donbass, Ukraine. Mater. XIV SEL Congress. Roma (Italy), 2005, P. 41-42.
- 145. Beloshitsky P., Klyuchko O., Onopchuck Yu., Onopchuck G. Mathematic model for hypoxic states development for healthy people and ones with ischemic heart disease. High altitude medicine and biology: Mater. ISMM Congress. Beijing (China), 2004, V. 5, P. 251.
- 146. Beloshitsky P., Klyuchko O., Kostyuk O., Beloshitsky S. Peculiarities of high mountain factors influence on organism. High altitude medicine and biology: Mater. ISMM Congress. Beijing (China), 2004, V. 5, P. 250.
- 147. Klyuchko O. M., Kiskin N. I., Krishtal O. A., Tsyndrenko A. Ya. Araneidae toxins as antagonists of excitatory amino acid responses in isolated hippocampal neurons. X School on biophysics of membrane transport. Szczyrk (Poland), 1990, V. 2, P. 271.
- 148. Akaike N., Kawai N., Kiskin N. I., Krishtal O. A., Tsyndrenko A. Ya., Klyuchko O. M. Spider toxin blocks excitatory amino acid responses in isolated hippocampal pyramidal neurons. Neurosci. Lett. 1987, V. 79, P. 326-330.
- 149. Gonchar O., Klyuchko O., Beloshitsky P. Ways of myocardial metabolic disorders correctionathypoxiabynewpharmacological preparations. High altitude medicine and biology: Mater. ISMM Congress. Beijing (China). 2004, V. 5, P. 249.
- 150. Gonchar O., Klyuchko E., Mankovskaya I. Role of complex nucleosides in the reversal of oxidative stress and metabolic disorders induced by acute nitrite poisoning. Ind. J. Pharmacol. 2006, 38 (6), 414-418.

151. Gonchar O., Klyuchko E., Seredenko M., Oliynik S. Corrections of prooxidant antioxidant homeostasis of organism under hypoxia of different genesis by yackton,

ЕЛЕКТРОННІ ІНФОРМАЦІЙНІ СИСТЕМИ В БІОТЕХНОЛОГІЇ

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Метою роботи було узагальнити та проаналізувати використання електронних інформаційних систем у біотехнології для створення нових версій цих систем. Опрацьовано публікації стосовно систем різних типів, придатних для вирішення проблем у біотехнології. Подібні системи, які традиційно належать до біології і медицини, було класифіковано. Розглянуто перспективи їх застосування для розроблення в подальшому більш досконалих електронних систем.

Ключові слова: біоінформатика, електронні інформаційні системи, бази даних.

new pharmacological preparation. Acta Physiol. Pharmacol. Bulg. 2003, V. 27, P. 53-58.

ЭЛЕКТРОННЫЕ ИНФОРМАЦИОННЫЕ СИСТЕМЫ В БИОТЕХНОЛОГИИ

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Целью работы было обобщить и проанализировать использование электронных информационных систем в биотехнологии для создания новых версий этих систем. Изучены публикации относительно систем разных типов для решения проблем в биотехнологии. Подобные системы, которые традиционно относятся к биологии и медицине, были классифицированы. Рассмотрены перспективы их применения для разработки в дальнейшем более совершенных электронных спстем.

Ключевые слова: биоинформатика, электронные информационные системы, базы данных.