REVIEWS

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INFORMATION COMPUTER TECHNOLOGIES FOR USING IN BIOTECHNOLOGY: ELECTRONIC MEDICAL INFORMATION SYSTEMS

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The purpose of the study was to review mordern information systems elaborated for medicine and biotechnology. Classifications of modern medical information systems and detailed description of their different versions based on numerous publications are given. Electronic information system for the biochemical laboratory with individual patients' data protection was developed for the hospitals in Polissia region of Ukraine polluted due to Chornobyl accident is suggested.

Key words: bioinformatics, electronic medical information systems.

Information computer technologies are widely used in contemporary biotechnology, which needs more specialized electronic information systems. The importance of information technologies (IT) and computer technologies (CT) use in modern biotechnology is indisputable fact nowadays. Primary there were no elaborated electronic information systems (IS) with databases (DB) developed specifically for biotechnology — it was economically unjustified [1, 2]. Constructing technical information systems (tIS) with DB, IT professionals could use wide spectrum of mathematical methods [1-9]; they could take prototypes from physics and techniques, because tIS were elaborated primary for these spheres. Later such tISs were accepted from medicine, biology, chemistry and etc.; they had to be modernized and adapted for biotechnological tasks solution. Because biological sciences and technologies have their peculiarities, professionals need their own electronic IS with DB. So, for the construction of tIS for biotechnology we suggested to study the experience of medical tIS elaboration because of the following reasons. 1 medicine is one of the nearest spheres for biotechnology that demonstrates the great variety and quality of IS because of good finding (people take care about their health ever); 2 — for biotechnologists (as well as other professionals) there were not important from what IS to get the data for their work, if only this data were. Indeed, for the research work the real scientific data are necessary, independently on the source of their origin (in medical tIS there are lots of necessary data); 3 — therefore, for the construction of similar tISs for biotechnology, one needs to know the prototypes from medical tISs to develop the better ones, similar and even more suitable systems; 4 — in our originally constructed tIS, described at the end of this article, a biochemical electronic laboratory is added. According to this example, one can add to tIS all necessary segments: for biotechnology, and other ones; 5 — biotechnological applications in medicine are very important; 6 — finally, it is very useful for engineers in biotechnology to know the different types of medical tISs as prototypes for the success of their work. To give to professionals in biotechnology the possibilities to invent new IS versions more effectively, we decided to observe some medical tIS prototypes.

Diversity and variability of medical information systems. According to abovementioned, the types of medical

information systems were numerical and diverse in their construction. They were the most numeric in medicine in comparison with biology due to a good funding in medicine and health protection through over the world. Mathematic models that we described in our previous articles as well as published by other authors also may be used for ISs functioning or to be simulated in result of their functioning [9-79]. A spectrum of mathematic methods is used for the newest biomedical ISs elaboration [1, 11, 74, 76-140]. Databases content described in this article was obtained from the results of biological and medical observations and experiments [10, 12-17, 22-44, 47-49, 61, 68, 71–74, 79–85, 90, 93, 94, 104, 107, 109, 110, 113, 120, 126-148]. Indeed, all such tISs are network-based and linked with databases today [1-11, 25-71, 90-109, 112-119]. In our numerical previous publications [1-6, 18-37, 61, 62, 64-66, 75, 126-148]we have investigated repeatedly the various aspects of below described phenomena and processes.

Medical tIS described below demonstrated a great variety; we elaborated and offer their classification. Information for this classification we found in different scientific and technical sources published since 2000. In our list there are contemporary electronic databases with access to the Internet with information in biology and medicine, designed during the last 25 years.

Despite the diversity of such systems (and, accordingly, publications), it was possible to distinguish certain well-defined types of ISs

among them. It is necessary to emphasize that such classification in finished form did not exist in scientific and technical literature until 2008; so, it is original.

Thus, in medical IS with DB one could distinguish: medical ISs of general purpose, 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

Placing these ISs types in hierarchy, we followed the principle: the more publications contain modern scientific and technical sources about this type of systems — respectively, the higher its name is in our list. It means that the developers payed the most attention to them; consequently, they were the most popular in practice (in modern hospitals, laboratories and etc.) Apparently, the most often published works fall into the section "Medical IS of general purpose". This could be explained by the practical needs of clinical medicine, which requires the most such versions. When viewed this list 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" falls to the lowest number of publications. This does not mean that electronic medical DB were not important in medical practice. Such a pattern can 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 databases do not see them as

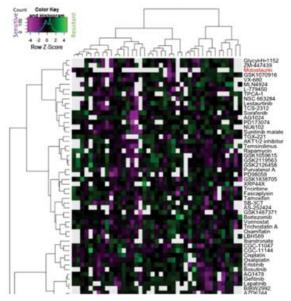


Fig. 1. Use of informatics in medicine: two-dimensional hierarchical clustering of drugs based on similarity of anti-proliferation effect profiles on breast cancer cell lines [73]

novelty, required for scientific publications. Our proposed examples of classification of the main IS types for biology and neurophysiology (as a branch at the junction of biology and medicine) were described in our previous publications [1]. Result of the use of medical "systems for scientific purposes" is illustrated on Fig.1. In result of contemporary informatics' methods use, two-dimensional hierarchical clustering of drugs based on similarity of anti-proliferation effect profiles on breast cancer cell lines was done as well as, in result, the conclusion about midostaurin action. Midostaurin suppressed the proliferation of TNBC cells among the breast cancer cell lines presumably through the inhibition of the Aurora kinase family. The precise study of midostaurin on cell growth would contribute to the development of the drug for the treatment of TNBC using computer technologies.

Some theoretical approaches for the construction of the largest groups of medical electronic tISs. As as it was noted, the most recent publications in the world according to our classification show that the most numerical ones are: "Medical IS of general purpose" and "Medical expert systems". Let's observe the information of these sections, which explains this fact.

Some theoretical data about the generalpurpose medical information systems. Today the Internet is used widely in clinical practice, medical research and education. Examples of its applications were, for instance, telemedicine, the collection and accumulation of clinical and experimental data, the making of electronic collections of professional literature, analysis of DNA and protein sequences of patients and distant learning for some medical courses, and etc. All of these applications required the development of electronic databases. The first medical ISs appeared in the 1970-th, and their main features, according to their performed functions, became established until the mid-1990-th. The "traditional" core of medical ISs was: clinical decision-making system, clinical record system (including patient records) and clinical databases [112]. During the first years of the XXI century, medical ISs demonstrated a real upswing in their development due to the numerous new technologies that have emerged in those years. In [78, 112] it was shown that the modern Internet provides opportunities for patients, their families, physicians to communicate with each other, to study new medical information and to exchange it. For these purposes there were established the centers for patients; these centers were equipped with electronic ISs, for example, the "eHealth system". It was calculated that the services of such electronic ISs in the USA during 2002 used, according to various estimates, from 73 to 110 million users (estimates were made for Medline (1966–2002), CINAHL (1982–2002), Cochrane Controlled Trials Register (till 2002), PsychInfo (1967–2002), and some others). The virtual capabilities of such systems were needed, in the first order, for people with disabilities and for lying patients.

Medical expert systems. The Internet provides good opportunities for the construction of powerful expert medical systems. In such systems, opportunities for the obtaining of information (OI) can be done rather cheaply, it is the best way for exchanging by large information volumes, to obtain variable information and even controversial one, from medical experts from different fields of medicine and from remote geographic regions. Clinical decision support systems (CDSS) have become used in medical practice more in recent years. The first such system, which has been widely used since 1970, has become the medical expert system MYCIN. After it, a number of systems were created for provision of access to medical information. interpretation of diagnoses, and so on. During these systems development two important problems were solved: choosing of methods for efficient system construction and data usage from the DB. For this 2 groups of methods were used — *automatic OI* and OI receiving in manual mode (manual OI).

The method of automatic OI (also called "Knowledge Discovering" and "Data Mining" — "knowledge acquisition") was relatively new method. His most important step was to extract abstract rules from a large number of cases. The most used automated OI methods were neural networks, discriminant and cluster analyzes, linear programming, evolutionary algorithms, and others [1-37, 41-148]. However, these methods were not considered as perfect due to the extremely complex algorithms that were not well developed. For example, during the data searching from the large DB, some data may be incorrect or not enough correct, and this would influence on the output rules. As a result, the huge efforts and expert time could be spent in

Consequently, most of the modern medical bases of knowledge refer to the *manual OI*, although knowledge bases designed for this method were usually small, referring to

very specific and relatively narrow areas of medicine. Manual OIs were elaborated usually in close collaboration with medical experts and engineers, sometimes it took a lot of time; it was important that the medical diagnosis is a complex cognitive process that medical experts are sometimes unable to formalize. Manual OI were not available everywhere, therefore, not all users outside of the health center could use these systems.

The Internet can solve these problems better than traditional platforms, since 1—the Internet is widely available; 2—Web browsers provide a common multimedia interface; 3—for expert systems developed software can be obtained from the Internet; 4—there are protocols for the interaction support between such expert systems. Experts can communicate online in real time; they can eliminate duplication of information, and etc.

"Medical ISs of general purpose". Let's observe some samples of electronic medical ISs. Some authors considered that ISs occurred spontaneously in hospitals and these systems need to be modernized in accordance with present day requirements. It is necessary to develop the general concepts of such systems and their modernization [1].

In [122] the principles of Web-system He@lthCo-op functioning have been described. It was noted that the healthcare industry is characterized by the need of close cooperation and information exchange between many professionals working to improve the health of patients at different times and often remote from each other in space. Modern IT and CT allowed us to make the systems through which such tasks can be solved. The He@lthCo-op modular Internet system has been constructed and implemented into practice, which makes possible the joint work of medical staff and transmission of confidential, protected information about the patient to remote sites. The He@lthCo-op system permitted to collect, maintain, and easily access patient information, at any time and from anywhere where access to the Internet was available. This function was not easy for implementation, since such information is completely heterogeneous, has different formats, it included not only medical data, but also personal and administrative information.

One of the main requirements for working with such data was to protect patient information in accordance with the current Health Insurance Portability and Accountability Act (HIPAA) that suppose friendly attitude of the nursing staff to

patient's and their data. Based on this viewpoint, various medical institutions have tried to establish procedures for conducting of their own standardized patient records, and subsequently to elaborate a complete electronic records' databases for patients. For such service it was necessary to construct united IS, which would be easy to use in different geographically distant medical institutions, to enter it outside of medical facilities if the patient moved to another country. He@lthCo-op system [122] solved the same problems. Internet had provided the ability to develop such systems with different scenarios, on different software and hardware platforms. At the same time till 2010, only a few clinical establishments had well-adapted Web-based ISs for electronic patient records, which makes it difficult for doctors to work with them if they are outside of this center. IS designed for the purpose of health care, should operate in environment with many different types of users, for example, a medical institution, technical staff, nurses, doctors and patients by themselves. All these persons should exchange heterogeneous multimodal medical data, documents, other information, operate through the system simultaneously or at different moments of time, within a single medical center or at different geographical locations, and there must be a system of feedback between patients, doctors and administrators. For such functions realization the Web-based systems and database-based systems were suitable; they are highly flexible, can easily transfer information to final user, can provide a friendly interface, have developed set of services and navigation tools. The system He@lthCo-op had exactly these characteristics (Fig. 2).

In other publication [124] an electronic IS called "eMAGS" (Medical Agent System) was described. According to performing functions it was similar to the previous He@lthCo-op system, but differs because it not only made medical records databases for patients, but also it was focused on the data streams exchange between different medical organs. The authors wrote that one of the main characteristics of modern medical ISs is the high level of cooperation between different medical institutions. The eMAGS system was an ontologically-based, multi-agent system that is designed to interact in a distributed medical environment without a certain boundary and traditional client server. The eMAGS was based on the messaging standard adopted today

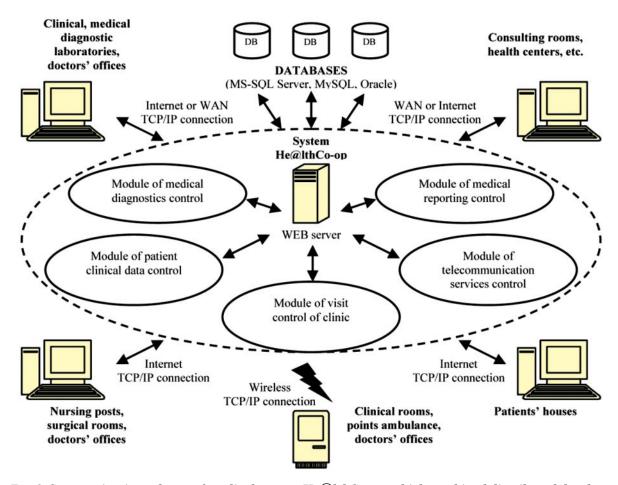


Fig. 2. Communication scheme of medical system He@lthCo-op, which combined distributed database repositories and various points of medical care provision [122]

in medicine and named HL7 (Health Level Seven) and facilitates the patient information transmission to healthcare organizations. Constructing this system, the authors took into account the fact that with the growth of even one medical center, the electronic service network and information transmission between its various components become more diversified and complicated with time. The health control was knowledge-intensive, divided into professional sub-domains, each of which may have its own dictionary, database and software; it could be multyplatformal, which significantly increases the complexity of this area. The authors paid attention to the fact that with such complexity increases also the fragmentation of information on patient detected by electronic system. The degree of fragmentation increased if the patient turns to the medical center periodically for a certain time. Recently, the peculiarity of medical ISs was that the user can contact with such system through mobile communication devices or through home monitors in the case of patients

at home. All this required the consolidation of information from heterogeneous data resources and has been called *interoperability* between these resources.

The situation of interoperability of medical ISs associated with the extraction of information from heterogeneous resources and work with them in real time. This situation was quite unique for ISs and it has no analogs in the industry, banking, insurance or other areas. With the quick growth of the Internet, the researchers and IT professionals have faced the problem of consolidating and managing of information in order to maximize the interaction and relevance of received information. Consequently, the key focus must be on integrating of the data from existing systems and making of useraccessible mechanisms for information sharing and distribution. The problem was that data from the disparate resources have different formats and they are incompatible often. The authors saw this problem solution in the use of federalized approach to databases, XML-

based integration, semantic meta-data-based integration of the data, in the creation and the use of a certain software samples, in the use of a single conceptual model or ontology, and in eGATE-type toolkits for transmission. For many problems solution, the popularity of ontologies had increased significantly — from the projects of academic data presentation to the commerce. Yes, commercial systems like CycSecure and EcoCyc have expanded the scope of ontologies. In their system eMAGS the authors could get flexible solutions through the use of multi-skilled mobile agents that provide active access, decryption, study and use of information presented in different medical ISs. eMAGS component HL7-RIM was the basic intermediary for data exchange between programs. eMAGS agents could be communicatively interconnected, since ontology establishes a single terminology for the domain (Fig. 3, a, b).

Medical expert systems. Using the above theoretical approaches, a medical expert system was developed [97]. The authors described their system which is based on three databases, client-server architecture and

invented by developers type of information processing management. To facilitate the knowledge presentation, data in DB and to obtain knowledge from the Internet an 8-bit encoding scheme and a weighting system were proposed. The system has been tested already in clinic. The authors set the following purposes: 1 — to create a medical IS for information processing and management system for it to facilitate the elaboration and maintenance of medical knowledge bases; 2 to maximize the information distribution and its following use by medical institutions and doctors; and 3 — to facilitate the process of decision making by medical expert systems. The authors described the method of control of Internet information processing, which they used to construct large databases of medical knowledge. The testing system was developed using Delphi 5.0 and Microsoft SQL Server 2000, it was available online for the testing during one year. The authors argued that their method and system made easier the operation by large volumes of medical knowledge.

Another Internet-based system was

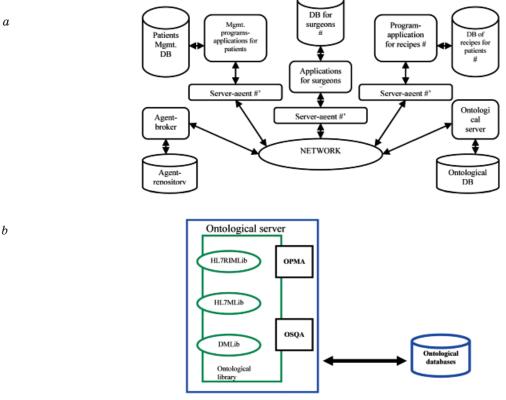


Fig. 3. eMAGS medical system [124]:

a — Architecture of eMAGS medical system. The essences of "agent" and "ontological" types were components of eMAGS system. Indications: # the greater number of such entities were supposed to be in medical institution; 'the essence of this type had a database and an interface for the user; b — Ontological server and its components

developed to select patients for clinical trials in oncology [103]. Large-scale clinical trials in the modern world are often multicentral, which means that they are based on different geographical points of the Earth, often in different countries. They are conducted to study effects of important potential medical preparations which could be recommended then for people treatment. For such a work it is necessary to provide the highest level of standardization, to record in databases numerous test results, and to fulfill a number of other specific requirements. Modern Internet technologies provided the opportunities for such work, although until the last days the patients' selections for tests carried out manually sometimes. Developers of expert system from the Moffitt Cancer Center, USA, described their expert system for patient selection [103]. The data about each patient were recorded to it, and if there are not enough data, the system offers additional tests. The system permitted the automating of selection process, the increasing the number of patient that can be selected (previously up to 60% of eligible patients were lost) with a significant reduction in cost of testing procedures. A user-friendly interface had been developed, which allows a healthcare professional to add test data and to make new selection criteria without the help of programmer. This system has been tested in oncological hospitals. This is extremely important because, according to statistics, only in the United States 550.000 people dies of cancer every year. For this sphere of medicine a large number of new medicals are developing and testing constantly. In case of successful results they come to patients immediately — thus for the newly developed medicals the shortest path from the laboratory to the patient was invented.

Electronic systems for the work with images. The following several ISs were designed for the work with images. There were some well-known methods for the work with images in medicine, for example, diagnosis of X-rays, ultrasound diagnostics, and etc. For techniques of images processing it was necessary to have few, sometimes few hundreds images even for one patient. So, a problem appeared concerning images recording and their ordering in DB with subsequent use.

An electronic medical system NORMA was elaborated in Genoa, Italy, for radiological center for the needs of radiotherapy [101]. It was designed jointly by the teams of physicists and radiologists in order to develop the most optimal schemes for the planning of treatment

by radiotherapy methods. The system was based on databases that contained, together with standard patients data, numerous images of tumors and areas of patients' bodies where is a risk of their occurrence. NORMA provided new for its time interesting opportunities for patients to record in DB and to visualize a large number of images made for tumor diagnosis and related body areas of risk. There was a possibility to study, to analyze, and to discuss such images by physicians and radiology physicists simultaneously in different loci of the system. NORMA had a client-to-server architecture and it is platform-independent. Internet technologies that make it easy to use it for people without special computer knowledge were used, due the commentaries at each step that help to user to perform the next actions. The system was subdivided into server based and client sides on Java software applications. For implementation optimization the project also included, in addition to TCP/ IP, another relevant protocol that organizes the data exchange and message control. Images for diagnoses were stored and removed from the appropriate DB or standard DB of DICOM (Digital Images and Communications in Medicine) through the connection DICOM-WWW, which allows to connect the normal Internet browsers used by NORMA system and DICOM software via the HTTP protocol. Browser requests were sent to the Web server connection via CGI (Common Gateway Interface). The DICOM software converted queries to DICOM messages and organizes the connection to the remote site of the DICOM Application system.

In [53] the authors described their developed web-based medical education system that simulates images. The system was elaborated for training students and doctors who work in design and processing of medical images. Using this system it was possible to train them for the work with X-ray, tomography, ultrasound and other images and documents. Internet technologies allowed ones to work with them online, in an interactive web — site environment. Some techniques for working with images, image processing algorithms and exercises for training in an interactive virtual laboratory were described in [53]. Each illustration has extended comments, including profound explanations of physics and math. For the work in the Internet a user-friendly interface was developed, trainings are held in MATLAB Web Server environment. Macromedia Director MX was used to develop an interactive animation

theory with graphical-oriented simulation. HTML and JavaScript were used to enable the user to apply these modules online in a web browser. The teaching quality grew due to the use of multiple choice questions, ability to analyze image data, and material submission according to module principles.

Another system for the work with images was elaborated for medical hospital in Shanghai, China [79]. The authors have developed a web — based system for interactive demonstration of electronic patient records. such as DICOM images, graphic images, report structure and therapeutic records for the hospital's internal network software and for the Internet. This system consisted on three main components, client-server architecture for patient data obtaining and authorization, and Internet-based system for data transmission. The system that visualized the data in the Internet includes multimedia display modules and remote control module for managing of software functions and for interacting with patient data. This system has been successfully tested twice during teleconsultations of patients with acute respiratory syndrome in the Shanghai Infectious Disease Hospital and Xinhua Hospital. During the consultations, doctors in area of infection control, and remote experts could interactively used this system to work with electronic images and patient records, which facilitated the correct diagnostics. The techniques developed by the authors provide new opportunities for making of images of patients' documents using Internet technologies and DICOM standards. This system could be used both in the intranet and in the Internet for tasks' solutions in telemedicine, teleconferencing and distance education.

Electronic systems for the work with medical documents. In publication from Brazil [51] it was upraised the problem of medical documents' processing. The availability of a huge number of medical documents in the modern Internet today is inconvenient for users, since it is difficult to find the right documents. Moreover, among them there are many documents with inaccurate and incorrect information, and documents without critical inspection of professionals. The authors suggested the MedISeek metadata model, which allows providing ones with medical visual information, including information on the properties, components, connections and image authorship. The model used webarchitecture and support of International Classification of Diseases and Related Health Problems (so-called ICD-10). The derivative metadata model was integrated into each medical image and specifies the semantics. Thus, the relevant information can be obtained directly from each image; the data integrity is stored in the Internet. Previous experimental results indicated that authorized users of the system can describe, store and transmit medical images and related diagnostic information (Fig. 4).

Some principles of medical documents processing are given in [119]. Concepts of automatic recognition of professional notions in medical informatics, the search for corresponding notions in the text are important tasks, as well as the task of medical documents obtaining from the Internet. In this work, the authors presented the software called the "keyphrase identification program" (KIP) to identify the main concepts from medical documents. KIP combined two functions: the extraction of nouns from phrases and identification of key phrase. Then, for nouns from the selected phrases from medical documents the weight were given, which depends on how important they are to medical documents and on the specificity of their medical domain. Experimental results demonstrated that the proposed extractor of nouns from phrases is effective in identifying of noun phrases of medical documents that is why it is suitable for identifying of important medical conceptual terms.

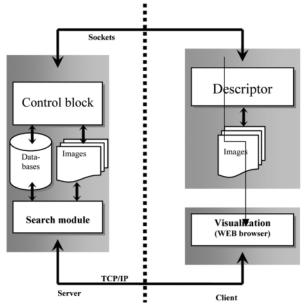


Fig. 4. The scheme of MedISeek subsystems [51]

The exchange of information streams in medical networks reveals the serious problem of medical vocabulary and related dictionaries standardization. The following electronic dictionary systems were elaborated for this problem solution [100]. During the past twenty years the WordNet system has been elaborated for the English-speaking countries; it is believed there is the most modern lexicon of modern English for its time. With the start of electronic medical information systems development, the Medical WordNet electronic lexical system, which virtually overlapped the sets of WORDNET vocabulary and medical terminology, began to be developed. The new Medical WordNet repository contains 3 large collections: 1 — forms of words used in medicine and structured according to the Princeton WordNet; 2 — medical-important suggestions called medical facts that were united into MedicalFactNet; 3 — records formed on the basis of nonprofessional questions, which refer to this system, combined in MedicaLFactNet. In such a way the developers have formed a new type of medical resources, which is based on the database related to the medical domain. The sentences were generated from WordNet. There are 2 "sub-body" sentences referring to MedicalBeliefNet or MedicalFactNet. The first type had to be evaluated by users – nonprofessionals, the second one — by medical experts, and the possibility of this type of double assessment of the system the authors saw as their great achievement. The results of the developed system implementation were examined during a small pilot experiment; the widespread use of this system was expected.

Electronic teaching systems in medicine. The following system related to electronic teaching systems in medicine [104]. Japanese developers have designed a multimedia educational Internet system for medical lectures that has friendly characteristics and relatively low price. The system has been elaborated using the RealSystem package with TCP/IP network. Lecturers could demonstrate their lectures and presentations during conferences with video and audio over the Internet. Each slide from video or audio resources was projected onto a high quality screen. The system use demonstrated good results in process of distant teaching (Fig. 5).

The system was developed for Japan, where in 2003 all universities, institutes and main hospitals were connected by gigabit Ethernet network with high speed (up to 1024 Mb/s) and wide data band. After the

systems have been upgraded from the point of view of compressing the data files to increase the streams' speed in the network, the transmission of high-quality video and images become possible via the Internet. It was noted that commercial "video-on-demand" system, which was elaborated earlier, could not broadcast only a variety of medical lectures and performances, but also to record images and synchronously with them to record audio files in user's library. If somebody needed to review the materials again, students or doctors could do it easily, as well as to study lectures from remote universities in a convenient place and time. However, the previously done "video-on-demand" system for 2003 was still quite expensive in order to install it in many universities in Japan. The newly elaborated system, based on the RealSystem and TCP/IP packages was less costable than previous ones; it was more convenient and easier in use, which makes it more suitable for wide spread use in universities and hospitals.

Electronic information system for monitoring of the population health in *Ukraine*. In our previous publications [1–6] we have already described how we developed some theoretical principles for the creation of technical electronic information systems (tIS) for biology and medicine, as well as the experience of practical developments of such systems. The next step was the development by Klyuchko O. M. the electronic technical system for environment monitoring [1], in particular the system called "EcoIS". Being a complex network system that permitted the improvement and relatively independent development of its segments, Klyuchko O.M. and Tsal-Tsalko V.I. at the next stage decided to expand the "EcoIS" system capabilities by adding a medical sector which is described below. This is especially important for the conditions of Ukrainian Polissia region, whose

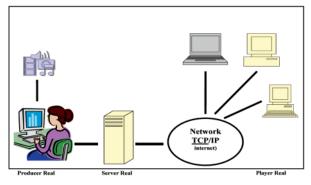


Fig. 5. The scheme of multimedia system for information spreading RealSystem [104]

environmental conditions have been worsened in many areas in result of Chornobyl accident pollution (1986) [1, 29]. Therefore, we have expanded the EcoIS functionality so, that it became possible now to monitor not only the presence of pollutants in the environment and the response to them invertebrate organisms, but also the monitoring of number of human health characteristics, including biochemical characteristics of organism functioning. Practice has shown that for health monitoring of the population living in adverse environmental conditions, it is necessary to organize and implement local IS diagnostic centers, electronic working places for individual doctors, formation of standard and at the same time flexible formats for diagnostic data recordings. At the next step it is necessary to unite subsequently such electronic working places in a network; initially — at the level of the clinical institution, and then at the higher level, up to the national one. The effectiveness of medical ISs depends in great degree on the maximal possible formalization of diagnostic information, which requires the active collaboration of engineers and doctors [1]. One application of IS functions was screening-filtering for a certain set of patients' diagnostic parameters during the mass screening and in the allocation of risk groups for a more complete survey. It did not require the high reliability of the primary diagnosis, since the selection threshold can be given with sufficient margin. For screening the fairly simple algorithms such as the type of tree of features or the calculation of some weighting metrics of input parameters could be used. More complex diagnostic programs — expert systems — were based on a certain knowledge base, which is formed by accumulation of experience in the application of other diagnostic methods. They used complex algorithms based on the analysis of links between features or based on neural networks models that can self-tune on some training sample, which makes them virtually universal. To obtain objective diagnostic information the texture analysis of tomograms or ultrasound images, automatic allocation of objects, definition of characteristics with subsequent identification and classification by images recognition systems could be used.

Such computer diagnostic systems could be used both together with IS with electronic disease history, as well as autonomously, for example, directly in diagnostic centers or in the reception rooms of medical specialists. Together with diagnostic equipment, the special applications that were optimized for narrow use may also be used — optimal visualization settings, making of slices or projections, 3D simulation, image matching, formatting of image groups for printing [1]. All this made free diagnostic physicians and auxiliary staff from the routine operations, it is greatly simplified, facilitated and accelerated their work. In recent years, such software products had been actively developed and implemented somewhere in Ukraine [1]. The task of fulfilled work was to develop the system segment for monitoring of number of medical characteristics of population health state, organism biochemical parameters, patient electronic medical card, and etc. for the regions of Ukrainian Polissia and to suggest an adequate technique for information protection in such system.

Development of the software complex "General medical database" in the "EcoIS". A medical IS with patients database (as well as healthy residents) we developed for the use in ecologically polluted areas of the Ukrainian Polissia (in particular, town Novohrad-Volynskyi and its surroundings) [145]. This IS we called "General Medical Database". During this IS development two important features of Polissva region were taken into account. The first one — is radioactive contamination as a result of Chornobyl accident, and in such areas it is extremely important to conduct long-term monitoring of both the ecological situation and the population health in order to reduce indicators of morbidity and mortality [29]. The second one — the region is characterized by the large forest areas, small density of population living in remote, hard-to-reach small settlements. In such conditions, it is problematic not only quick medical care, but also medical care by itself, because even simple communications between settlements are difficult. Modern IT technologies help to achieve significant success in such problems solution.

Our developed networked IS with databases for population medical care and monitoring of their health status was called "General medical database" within the greater our IS — "EcoIS" [145]. The following elements of this IS have been developed:

- 1 medical databases;
- 2 electronic medical card of examined person (or patient);
- 3 electronic key for the protection of private individual health information (person or patient being examined), since such information is confidential.

Below the information on each element of this IS development is suggested.

Development of electronic medical database in the "EcoIS". An electronic medical database is an electronic analogue of patient's traditional medical card. This was a repository of records, each of which contains medical information: complaints, diagnosis, prescribed medicals, results of laboratory tests, medical indicators, and etc. [145]. Each entry can contain text information and tabular data, graphic images, as well as attached files of any type (spreadsheets, documents in.PDF format other). In addition, records may contain medical images in DICOM format (CT, MRI, ultrasound, etc.). Developed electronic medical database may be available in any hospital of Ukraine with available Internet; the data loss is prevented.

Design of algorithm and code for electronic medical database. At the beginning the program interface was developed; it includes about 20 forms. The structure of interaction between the forms is shown on Fig. 6.

"Form1" is a "Greeting" interface; it also has a function of entry to the main program with reading the data of electronic key and patient's identification number, if it is already recorded into the database. A code for reading of "doctor ID" from the electronic key was written also.

In Form2 there are several tabs according to the physician's access point to the information. For example, the doctor-radiologist can not see the history of the patient from infectious department. The first tab shows patient data. If the electronic key with the access level of "Registration", then the user can add or edit the personal data of the patient. Other doctors can see only the information without editing.

On the other tabs there are automated workplaces (AWPs) of defined physicians (other name is "electronic work places" — EWP). The doctor can open the history of disease in any moment from his AWP and review it. The search is possible according to the date of database entry.

The tab "Laboratory" is the entry to biochemical laboratory and to results of patient biochemical analysis. On this tab there are several buttons that cause appropriate forms to save or to view the results of patients' tests (Figs. 6-9).

Tables MySQL and interaction of C# with databases. Sometimes it is necessary to connect these different technologies. For example, to write an offline client for CMS [1], who works using MySQL, development of local database /

program that uses it without any productivity limitations due to a free version of Microsoft SQL. Let's describe how the works on MySQL and.NET connection were done [145]. Navicat8.1 for MySQL was used to simplify the work with MySQL — there are free versions of Freeware. Of course, it could be completely replaced with MySQL Command Line Client.

It is necessary to install correctly the software on personal computer (PC). This is described in details on the MySQL site — put the studio, MySQL, and then put MySQL. NETConnector. After that, one need to create a project that can use MySQL Connector for the work with databases. We have to launch the studio, to create a new project — Windows. Forms, the language C #. After that we add Reference to the Mysql.Data component (rightclick -> Add reference). Now the namespace Mysql.Data is available for us. From it we will use MySql.Data.MySqlClient — we have to add the corresponding directive "using".

Listing of program "Connection". The process how to write the code correctly for the connection with database has been demonstrated in listing "Connection". In it the words marked by "italic" were written in Ukrainian (fragment of code).

Listing of program "Connection":

```
// connection data
   string MySQL host = "localhost";
   string MySQL_port = "3306";
   string MySQL_uid = "root";
   string MySQL_pw = "nopassword";
   MySqlConnection Connection = new
MySqlConnection("Data Source=" + MySQL
host + ";Port=" + MySQL port + ";User Id="
+ MySQL uid + ";Password=" + MySQL pw +
";");
   MySqlCommand
                       Query
                                     new
MySqlCommand();
   Query.Connection = Connection;
   try
   Console. WriteLine ("Connection with the
database server");
   Connection.Open();
   catch (MySqlException SSDB_Exception)
   Console.WriteLine ("Check server
settings! \n: "+ SSDB_Exception.Message);
   return;
   Console.WriteLine("OK");
```

To save information and for its subsequent search, it is necessary usually to design a

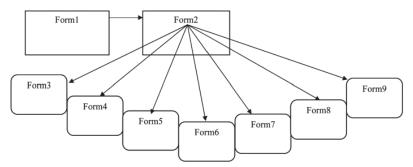


Fig. 6. The structure of software complex "General medical database" [145]

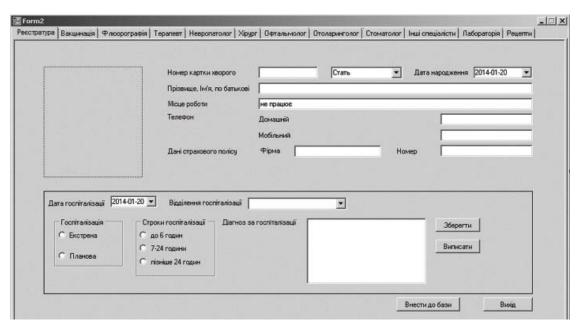


Fig. 7. Form 2, the tab "Registration" [145]. The original interface was designed in Ukrainian

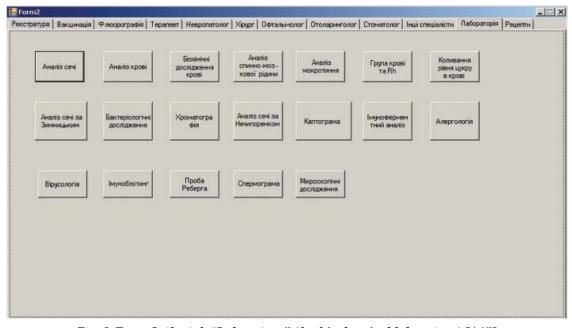


Fig. 8. Form 2, the tab "Laboratory" (for biochemical laboratory) [145].

The original interface was designed in Ukrainian

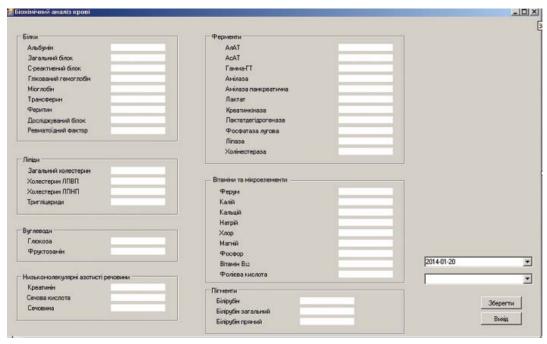


Fig. 9. Form 6, the tab "Biochemical analysis of the blood" [145]

The original interface was designed in Ukrainian

database in tables [1]. For this purpose MySQL was used. In the process of programming, the following tables were done: "Patient", "Doctor", "Hospital", "AccessLevel" and others (for each tab — program and form was done). The table "Patient" have been recorded the general information about patient (name, home address, telephone, other contact information, hospitalization time, referral department), as well as his ID, which permits to make a search in corresponding database according to the history of disease. In tab "Hospital" there are the data about hospital where works the doctor, who input patient data records into the database (contact information of admission and related physicians, etc.).

Construction of electronic key for the protection of medical data in "EcoIS". To protect the patient personal data in our IS, the method of program protection with the help of a hardware key was applied. Using this method, the confidential information about the health of examined person (the patient) was protected. The need to protect such confidential information arises particularly in the case of long-term monitoring of health indicators for the large numbers of people in regions with polluted environment (Figs. 10, 11).

Many specialized software packages use this method of hardware key. After the purchasing of the program, the author or distributor sends to user a physical device,

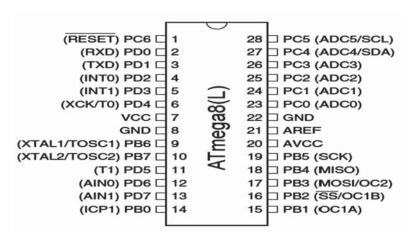


Fig. 10. ATmega8 used for the hardware key construction [145]

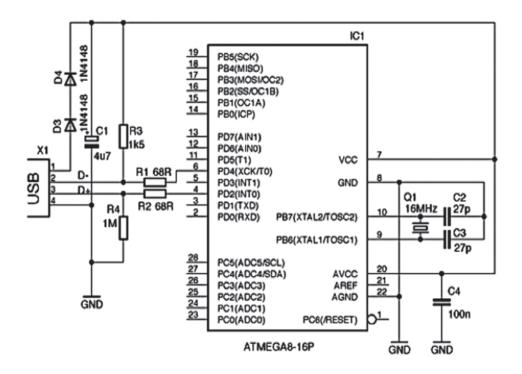


Fig. 11. The principle scheme of hardware key [145]

which is connected directly to the USB port — this is the hardware key. This is direct protection of programs from copying. The hardware key is a chip with some information that can not be reached (except as software), because it is impossible to look into this "black box". Most often, the hardware key does not have installed physical memory, but microcontroller that functions according to its inside program. So, a hardware key is a "black box" with unknown algorithm. This allows protecting software effectively against hacking.

To make the original electronic key we need a microcontroller and a circuit that implements the USB interface. We used Atmega microcontrollers. For them free software is available, and they have a low price in comparison with analogs. For the key the ATmega8 microcontroller was used because it does not include the internal USB function — we implement the USB function independently. We picked up the TQFP case.

Principal scheme of hardware key and code. Let's describe how to work with USB port, since operations with this port are not an easy task. We used the existing V-USB development, it was necessary only to make the circuit. This scheme is quite simple [145] and includes USB stick, microcontroller ATMEGA8, 2 diodes to reduce the voltage to the microcontroller since USB gives a voltage 5V. For proper

microcontroller operation at 16 MHz on legs, the microcontroller should be fed 3.3 V. For key operation we needed 4 resistors and 3 capacitors (the cost is enough low). Also microprocessor has to be programmed using appropriate program. The listing below demonstrates how to transfer the data that are into the operative memory of the microcontroller (fragment of program code) [145].

program code) [145].
 Listing of data transfer program
 uchar usbFunctionRead(uchar *data, uchar
len)
 {
 if(len > bytesRemaining)
 len = bytesRemaining;
 eeprom_read_block(data, (uchar *)0 +
currentAddress, len);
 currentAddress += len;
 bytesRemaining -= len;
 return len;
}

In the main PC program the following code for information reading from microcontroller should be written:

MyUsbDevice = UsbDevice. OpenUsbDevice(MyUsbFinder);

if (MyUsbDevice == null) throw new Exception("Device Not Found.");

IUsbDevice wholeUsbDevice =
MyUsbDevice as IUsbDevice;

if (!ReferenceEquals(wholeUsbDevice,
null))

```
wholeUsbDevice.SetConfiguration(1);
   wholeUsbDevice.ClaimInterface(0);
     UsbEndpointReader
                              reader
MyUsbDevice.OpenEndpointReader(ReadEnd
pointID.Ep01);
   byte[] readBuffer = new byte[1024];
   while (ec == ErrorCode.None)
   int bytesRead;
   ec = reader.Read(readBuffer, 5000, out
bytesRead):
    if (bytesRead == 0) throw new
Exception(string.Format("{0}:No more bytes!",
ec));
    Console.WriteLine("{0} bytes read",
bytesRead);
     Console. Write (Encoding. Default.
```

If there were no information from microcontroller within 5 second we considered that all information was accepted.

Console. WriteLine(" $\r \nDone!\r \"$).

GetString(readBuffer, 0, bytesRead));

Thus, in present publication the examples of highly developed technical information systems with databases elaborated for medicine were observed. The data from their databases and other their abilities it is possible to use in biotechnology as well as to use this experience for the construction of new information systems in this branch. For the solution of this problem the methods of modern informatics and computer sciences were used. The use of such information computer systems can be applied for the exploring of complex unexplored objects (databases of biological cell receptors, and etc.) in situations where the use of traditional methodologies is either complicated or too expensive.

At the beginning of article the scheme with classification of modern medical information systems is presented as well as detailed description of medical information systems' different

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versions on the base of more than 150 scientific and technical sources examination. Electronic information system with biochemical laboratory and personal patients' data protection developed by the authors for hospital in Polyssia region of Ukraine polluted during Chernobyl accident is suggested as well. This software complex was called "General medical database"; it has been elaborated as a segment of our primary developed "EcoIS" system. To do this, we developed our own original DBMS-based program and its protection using a hardware key based on the AVR ATmega8 microcontroller [145].

The main details of the software complex "General medical database" are described in present article [145]. A block scheme of interactions between program forms is shown, and the connection of the C # language and MySQL database management system using MySQL Connector is explained. During the development of the electronic system for protection of the software complex "General medical database" in the "EcoIS" there were developed our own original programs on the basis of database management system (DBMS), protected with the help of a hardware key based on the microcontroller AVR ATmega8. The main stages of design of a hardware key used for the protection of personal medical data in the database were described. There were presented its electrical circuit and software with the help of AVR Studio programming environment. Also there were explained the linking of the electronic key with the software complex using the library LibUSBdotNET (the library has become standard in the programming languages C, C ++). All recipes issued by doctors can be stored in the developed databases, their falsification is impossible and, therefore, all relative information can be checked by pharmacists. Almost a dozen programs — applications were used to fulfill the project. Implementation of the main program was under the Windows 8 on the.NET Framework 4.5 platform. The developed program can be installed on professional PC and used for the connection with databases in remote locations from hospitals.

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ІНФОРМАЦІЙНО-КОМП'ЮТЕРНІ ТЕХНОЛОГІЇ ДЛЯ ВИКОРИСТАННЯ У БІОТЕХНОЛОГІЇ: ЕЛЕКТРОННІ МЕДИЧНІ ІНФОРМАЦІЙНІ СИСТЕМИ

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Мета роботи — дати огляд сучасних інформаційних систем з базами даних, розроблених для медицини та біотехнології. У статті наведено класифікацію сучасних медичних інформаційних систем та детальний опис їх різних версій. Подано також опис розробленої електронної інформаційної системи із захистом персональних даних, призначеної для використання в біохімічних лабораторіях лікарень в районі Полісся України, забрудненого внаслідок аварії на Чорнобильській АЕС.

Ключові слова: біоінформатика, електронні медичні інформаційні системи.

ИНФОРМАЦИОННО-КОМПЬЮТЕРНЫЕ ТЕХНОЛОГИИ ДЛЯ ИСПОЛЬЗОВАНИЯ В БИОТЕХНОЛОГИИ: ЭЛЕКТРОННЫЕ МЕДИЦИНСКИЕ ИНФОРМАЦИОННЫЕ СИСТЕМЫ

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Цель работы — дать обзор информационных систем с базами данных, разработанных для применения в медицине и биотехнологии. В статье приводится классификация современных медицинских информационных систем и детальное описание их различных версий. Дается также описание разработанной электронной информационной системы с защитой персональных данных, предназначенной для использования в биохимических лабораториях госпиталей в Полесском регионе Украины, загрязненном вследствие аварии на Чернобыльской АЭС.

Ключевые слова: биоинформатика, электронные медицинские информационные системы.