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METHODS OF EFFECTIVE TEACHING BIOINFORMATICS IN MEDICAL ACADEMIC SETTING*

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Вища медична освіта є вимогою сучасності, що потребує переосмислення методів і форм навчання, а також принципів та підходів згідно із сучасними досягненнями науки і техніки. Пріоритетний напрям трансформації вищої медичної освіти – підготовка компетентних фахівців, спроможних відповідати на виклики часу, готових до самовдосконалення та постійного розвитку. Підготовка фахівців на третьому освітньо-науковому рівні вищої освіти сьогодні потребує форм та методів навчання, спрямованих на практичне використання отриманих знань.

Key words: біоінформатика, діяльнісний метод, метод задач, метод кейсів, медична освіта.

Higher medical education is a prerequisite of the present, requiring re-consideration of teaching methods and forms, as well as principles and approaches in accordance with the latest advances in science and technology. The priority direction in the transformation of higher medical education is training the competent specialists, capable of responding to the challenges of time, ready for self-improvement and continuous development. Training of specialists at the third educational and scientific level of higher education today requires forms and methods of training, aimed at the practical use of the knowledge gained.

Key words: bioinformatics, activity method, task method, case study, medical education.

The analysis of recent studies and publications on this problem has shown that the didactic foundations of the development and implementation of innovative pedagogical technologies are reflected in various fields in the research works of leading Ukrainian scientists: M. Zhaldak, Y. Mashbytsia, N. Morze, Yu. Atamanchuk [1], R. Horbatiuk [4], R. Hurevych [5]. Special attention of researchers is attracted to the issue of application of computer technology in the process of training [4, 5, 10, 11]. The main achievements of bioinformatics, pharmacogenetics are described in detail in the works by I. Kaidashev [6, 7]. The problem of teaching bioinformatics at the third educational and scientific level requires an updated approach and a scientific substantiation of pedagogical conditions that would ensure the effectiveness of the educational process.

Our analysis of the studies by the domestic scientists gives grounds to assert that the didactic basis of teaching for postgraduate students is not sufficiently reflected in the scientific literature, and the level of methodological provision of teaching the disciplines of general scientific and research cycles at the third educational and scientific level of higher education is not adequately developed and needs further study of the fundamental aspects in its

implementation.

The aim of the research is to highlight the main advantages of using teaching methods, differentiated by the level of independent mental activity, when teaching bioinformatics at the third educational and scientific level of higher education.

The subject "Bioinformatics" is a component of the educational and scientific program of training specialists for the third level of higher education in the field of training 22 – Healthcare (specialties 091 – Biology, 221 – Dentistry, 222 – Medicine) at Ukrainian Medical Stomatological Academy, consisting of lectures and practical lessons, which deals with specific problems on experimental biology and the approaches, methods, techniques for their solution by modern methods, provided by specialized computers.

Didactic principles, updated by the modern tendencies of the information society, should change the vector of action from the reproductive mastering of a large amount of theoretical knowledge to the ability to apply it in everyday life and professional activities. Today, not only knowledge, but also the awareness of where and how to apply it, becomes necessary, in addition, any data lose their significance over time [2].

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The current issue is the search, interpretation and creation of new data, that is, the focus on the outcome of the activity. Didactic principles of higher education should be aimed at linking the theory with practice and science, the availability of scientific knowledge, the combination of individual knowledge with the ability to work in the team. For medical students at the third educational and scientific level, important elements of the didactic system are activity, consciousness and autonomy in education. One of the most effective methods of training to implement this goal is the activity approach. Activity oriented learning involves mastering skills, first of all, their new types: educational, research, design, creative, and others. As a result, actual knowledge will be the result of working on tasks combined into an effective methodological system. And when choosing tasks, it is necessary to take into account that when solving a learning problem, the subject of education independently formulates the problem, finds the algorithm for its solution, solves and tests the correctness of this decision. Thus, the permanent resolution of such educational tasks is transformed into a systematic independent search activity.

For example, task 1: Study the following biological sequence databases:
 MSNITIYDVAREANVSMATVSRVNGNPNVKPTRRKKV
 LEAIERLGYRPNVAVARGLASKKTTTVGVIIPISSIFYSEL
 ARGIEDIATMYKYNILSNSDQNMEKELHLLNTMLGKQV
 DGIVFMGGNITDEHVAEFKRSPVPIVLAASVEEQEETPS
 VAIDYEQAIYDAVKLLVDKGHTDIAFVSGPMAEPINRSK
 KLQGYKRALEEANLPFNEQFVAEGDYTYDSGLEALQHL
 MSLDKKPTAILSATDEMAGIHAHQDQGLSIPEDLDIIGF
 DNTRLMLMVRPQLSTVQPTYDIGAVAMRLLTKLM-
 NKEPVEEHIVELPHRIELRKSTKS in the databases
 GenBank and Protein Data Bank. Analyze the results. Find how the second amino acid chain is encoded in the text of saved PDB format sequence (using the UCSF Chimera software). In the JalView editor, save the resulting sequences in one FASTA file.

To accomplish the task, the following algorithm must be performed:

- 1) to search GenBank, you need to find the NCBI website (<http://www.ncbi.nlm.nih.gov/genbank/>). On this website you need to find BLAST (Basic Local Alignment Search Tool - a resource for finding local alignment) [3];
- 2) go for a search on the protein base (protein blast),
- 3) find the amino acid sequence from the indicated letters in the base;
- 4) copy the set of letters into the search bar and press the BLAST button;
- 5) evaluate and save the result; obtain detailed information on the sequence;
- 6) go to the Protein Data Bank database at [www.pdb.org.](http://www.pdb.org/);
- 7) enter the identifier in the search string, get the sequence information;
- 8) evaluate the received sequence, scroll the three-dimensional structure of the model in the browser, using the 3D View function, select models that are similar in amino acid sequence or structure, etc.;
- 9) open the UCSF Chimera window at <http://www.cgl.ucsf.edu/chimera/download.html>;
- 10) choose File / Fetch by ID, enter the sequence code;
- 11) evaluate the obtained model;
- 12) determine which sequence of amino acids the model corresponds to (in the Tools / Sequence / Sequence menu);

13) save the result through the File / Save PDB function.

The step-by-step use and complication of such tasks will, in our opinion, contribute to the formation of necessary skills and practical orientation of learning.

Forms of organization of educational activities for implementation of the activity approach are traditional: lectures, practical classes, self-directed and individual work [4, 11]. Hence, for individual work, we offer task 2 for analysis, synthesis, structuring of information: Create a library of articles on the topic of your research in Google Scholar. In the international Scopus database, find the h-index of scientists you quote in your research and analyze their work.

Performing such type of tasks forms the ability to think critically and determine the reliability of the information that can be used for further scientific research. Increasing the complexity of the tasks performed will contribute to the formation of work experience and increase the level of the formation of computer literacy in general [9, 12].

To study certain topics of the subject, we used the method of tasks, the essence of which is the teacher's organizing the process of mastering knowledge through structuring the educational material in the form of a sequence of tasks that have a certain logical connection with each other. The PhD student, following this chain from one task to another, is included in the active process of self-mastery of knowledge. The list of tasks is quite extensive: tasks based on a clear algorithm; tasks requiring changes to the basic algorithm and simple mental activity; tasks in the reproduction of real situations that require a solution (research problems of increased complexity). Objectives based on a clear algorithm ensure the integrity of the mastering the corresponding actions. Correctly mastered and automated actions on the basis of algorithms, allow to form appropriate skills and abilities to successfully solve non-standard tasks [8]. When studying the topic "Alignment of biological sequences" the teacher needs to use special software tools to explain the principles of this process. In our opinion, this problem is the most effectively implemented through the appropriate actions. To explain the principles of the ClustalW and MUSCLE programs, we use the dot matrix principle. Alignment of closely related sequences is a rather simple task and can be produced by visual analysis. The purpose of the tasks based on the algorithm in this case is to ensure the integrity of mastering the relevant actions [3].

For example, task 3: Using the matrix principle, align the two sequences 1: FTFTALILLAVAV and 2: FTFTALITLAVTV.

Action algorithm:

- 1) two aligned sequences are written as a row and column of the table;
- 2) all identical nucleotides (or amino acids) are marked with dots in the corresponding cells of the table;
- 3) dots are combined in a line.
- 4) further – in the event that two sequences are identical, the dots will be in each cell on the diagonal of the table. If two sequences have substitutions but do not have spaces, then the dots will be in most cells on the diagonal of the table; if in the analyzed sequences there is a gap, then the diagonal is shifted vertically or horizontally.

Task 4: Based on the Nidman-Wunsha algorithm, align the two sequences 1: FTFTALILLAVAV and 2: FTFTALITLAVTV.

Action algorithm:

- 1) the aligned sequences are written as the first row and the first column of the matrix table;
- 2) cells with identical amino acids are assigned a value of 1, and cells with different amino acids;
- 3) determine the maximum possible sum of numbers in all cells at all possible steps through the matrix top-down down from left to right;
- 4) starting from the upper left cell for each next cell of the matrix the maximum possible estimate is determined, as if the aligned sequences ended in this position. For this, the maximum number of the column row from the top to the left of this cell is added to the initial number of the cell (0 or 1).

Next we offer to use the ClustalW and MUSCLE programs to align the biological sequences.

Task 5: Use the ClustalW program to align two biological sequences.

Action algorithm:

- 1) enter the web server browser web page <http://www.ebi.ac.uk/services>;
- 2) select the DNA & RNA block (genes, genomes & variation) and go to the page containing the programs of this block;
- 3) select ClustalW2 and go to the page with the window of the program;
- 4) for the amino acid sequences select the option Protein, and for the nucleotide – DNA;
- 5) insert a set of sequences in the window;
- 6) with the help of the Alignment option, select the type of alignment: slow or rapid;
- 7) using the option of DNA weight Matrix, select a matrix replacement, Gap Open – a penalty for the beginning of the break, End Gaps – a penalty for the end of the gap, Gap Extension – a penalty for the length of the gap;
- 8) click “Submit”.

We gradually complicate the task and suggest solving the previous task using the MUSCLE program with the following options:

1. Output Format – it selects the format for the file containing the result of multiple alignment;
2. Output Tree – it determines whether a tree will be displayed; if so, after which iteration.
3. Output Order – it defines the order in which the sequences will appear in the final alignment.

As a result of this type of assignment, post-graduate students memorize the techniques of search operations for their correct execution on a sample basis.

As a modern means of studying at a higher educational institution, the method of case study is actively used, the main purpose of which is to create such a situation by the teacher, when PhD students themselves have to make a decision.

Case is an event that actually took place in a certain area of activity and is the basis for discussion. When using the case, the participants are given a preliminary opportunity to get acquainted with the list of circumstances underlying which are real or imaginary situations. The description of this situation simultaneously covers not only a certain practical problem, but also actualizes a certain complex of knowledge that must be mastered during its solution. There are the following variants of application of the method:

- diagnostics of the problem;
- diagnostics of one or several problems and participants' workout of ways of their solution;

- assessment by participants of existing actions regarding the solution of the problem and its consequences.

In each of the following options, the learning process is carried out by the teacher's providing information in the form of a problem or a series of problems. This information can be presented in a documentary, pre-prepared form or by means of verbal and visual means (slides or video materials). Upon completion of the exercise, PhD students offer their work, which can be the basis for the discussion.

Preparation for a class using a case method should be consistent with a number of methodological conditions, in particular:

- the situation should be adapted to the knowledge that the teacher plans to update;
- presentation of information must be logical, consistent with detail, and information itself must contain a problem that PhD students may encounter in their professional activities;
- the problem solved by the teacher should have several options (this circumstance is especially important for large groups);
- information can be provided by hand-out material or multimedia presentations, video presentations, etc.
- for discuss the audience needs to familiarize with the material;
- it is necessary to choose the optimal homework, which will include a review of additional literature and information from Internet resources, etc.

For example, during the study of the topic “Genome Sequencing”, PhD students are suggested to study the issue of synthesis of peptide analogues and their biological activity.

We have divided the study of this issue into the following stages:

- 1) individual study of the problem under consideration (extra-curricular activities) with the help of the proposed list of sources, including articles in medical journals, Internet resources, information from the textbook;
- 2) classroom discussion of the method of a phased study of a solid mixture with the subsequent study of individual fractions, which is an accepted method for the separation of peptide mixtures;
- 3) discussion of the impossibility to use this method for separation of certain mixtures;
- 4) discussion of the essence of the alternative method for the separation of peptide mixtures proposed by Falk and Rotzschke in 1991 [6, 7];
- 5) division of the audience into groups;
- 6) discussing the advantages and disadvantages of each method;
- 7) general discussion, evaluation of the results of work.

This method of teaching may be an element of individual consultation, a credit test, when PhD students are asked to explain individual questions. The results of the method is necessarily analyzed by the teacher.

Conclusions. In the educational process at the third educational and scientific level of higher education in teaching the subjects of general scientific and research cycles, it is feasible to use tasks aimed at using knowledge in practice and real life situations, the content of which is presented in a non-standard form and requires the analysis of data or their interpretation, the formulation of conclusions or the consequences of various changes.

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