MINISTRY OF EDUCATION AND SCIENCE OF THE RUSSIAN FEDERATION
Federal state autonomous educational institution
of higher education
«Far Eastern Federal University»
(FEFU)

SCHOOL OF BIOMEDICINE

«AGREED»
Head of education program
«General medicine»
_____ Khotimchenko Yu.S._____
(signature) (Full name)
«09» of July 2019

«APPROVED»
Director of the Department of Clinical Medicine
_____ Geltser B.I._____
(signature) (Full name)
«09» of July 2019

WORKING PROGRAM OF ACADEMIC DISCIPLINE (WPAD)
«Molecular Genetic Technology»
Education program
Specialty 31.05.01 «General medicine»
Form of study: full time

year 5, semester A
lectures 18 hours
practical classes 36 hours
laboratory works not provided
total amount of in-classroom works 54 hours
independent self-work 18 hours
control works ()
pass-fail exam year 5, semester A
exam not provided

The working program is drawn up in accordance with the requirements of the Federal state educational standard of higher education (level of training), approved by the order of the Ministry of education and science of the Russian Federation from 09.02.2016 № 95.

The working program of the discipline was discussed at the meeting of the Department of fundamental and clinical medicine. Protocol No. 8, 09 of July 2019

Authors: prof. N.B. Serebrenaya, PhD Kumeiko V.V.

Annotation

The discipline "Molecular Genetic Technology" is intended for students enrolled in higher educational program 05.31.01 "General medicine", course included in the curriculum as a variable discipline of choice, implemented at the 5th year , 10 term. Total complexity of the discipline is 72 hours, 2 credit units.

In the work program developing, the Federal state educational standard for higher education 31.05.01 specialty “General Medicine” (specialty level) was used.

The course program based on basic medical knowledge gained by students:

CPC-7 - the readiness to use basic physical and chemical, mathematical and other natural science concepts and methods in solving professional problems;

PC-20 - the readiness to analysis and public presentation of medical information based on evidence-based medicine

PC-21 - ability to participate in researches;

PC-22 - the willingness to participate in implementation of new methods and techniques aimed at protection of public health.

Discipline is logically and meaningfully associated with such courses as "Biology", "Computer science, Medical informatics", "Biology", "Biochemistry", "Histology, Embryology, Cytology", "Pharmacology", "Clinical biochemistry", "Biochemistry pathological processes”, “Clinical and laboratory diagnostics”, “Immunology”.

Discipline goal: preparing students for research activities related to the modeling of biomolecules, as well as complex molecular systems: complexes, solutions, interface surfaces

Tasks:

1) acquaintance with modern achievements in the field of computer modeling of the dynamics of biomolecular objects and systems;

2) training in work with modern databases, software packages on molecular modeling and molecular dynamics using high-performance computing systems

3) mastering modern methods of molecular modeling of biostructures.

4) readiness for professional operation of modern research equipment and instruments.

"Molecular Genetic Technology" is an important discipline for the preparation of students of the 05/31/01 "medicine". it is designed to expand the methodological arsenal of the student and teach him to use modern tools that have emerged in the field of modern biology and medicine. in connection with the rapid development of methods for conducting experiments in silico, it is necessary to develop the ability to apply these methods for the effective conduct of biochemical, pharmacological and medical research.

to successfully study the discipline "Molecular Genetic Technology" the following preliminary competences should be formed for students:

As a result of studying this discipline, students form the following general cultural and professional competencies:

Competence code and formulation	**Stages of competence formation**	
CPC-7 - the readiness to use basic physical and chemical, mathematical and other natural science concepts and methods in solving professional problems	Knows	– place and role of molecular modeling in medicine; – main concepts, definitions, methods and approaches used in molecular genetic studies in medicine; – use of molecular genetic technologies in pharmacology and clinical medicine; – biomedical problems solved by approaches of molecular genetic modeling
	Is able to	– formulate problems of molecular genetic studies in medicine
	Possesses	– the main principles of molecular genetic research organizing in medicine
PC-2 - the ability and willingness to conduct of preventive medical examinations, clinical examinations and dispensary observations;	Knows	– the main principles of medical examinations in order to conduct genetic research
	Is able to	– organize medical examinations in order to conduct genetic research
	Possesses	– the main skills of medical examinations in order to conduct genetic research
PC-21 - ability to participate in researches;	Knows	– techniques for molecular genetic studies in medicine
	Is able to	– how to plan molecular genetic studies in medicine;
	Possesses	– skills to plan molecular genetic studies in medicine;

STRUCTURE AND CONTENT OF THEORETICAL PART OF THE COURSE (18 hours)

MODULE I. Biomolecular modeling and simulation (6 hours)

Section 1. Use of computer technology in bioorganic chemistry, biotechnology and molecular pharmacology.

Theme 1. Introduction in computer modeling of biomolecules structure and history of molecule visualization (2 hours)

Introduction to the discipline. Subjects of the course. Basic concepts of molecular modeling. Units of measurement: mass, energy, time. Number of particles in a simulated molecular system. Effective solvent metering. Periodic boundary conditions. Force fields. Functional types of interaction. Non-valent interactions: van der Waals and Coulomb forces. Circumcision radius Combination rules. Screening of the Coulomb potential. Algorithms for computing non-valent interactions. Efficient algorithms for finite radius of interaction. The most common force fields.

Active and interactive methods: problem lecture, lecture visualization (2 hours.).

Theme 2. Modern databases on biomolecules structure (4 hours.)

The potential energy surfaces. Minimum, transition state and intermediate. Hessian and its use for points identification. Global and local geometry minimization. Algorithms for local minimization. The minimizer orders. Minimizers of zero, first and second order. The method of simplexes and bijections. Gradient following method conjugate gradient method. Newton and Newton-Raphson Method. Algorithms for global geometry minimization. Monte Carlo method.

Metropolis criterion. General ideas about the genetic minimization algorithm.

Active and interactive methods: problem lecture, lecture visualization (3 hours.).

MODULE II. Protein structure modeling (6 hours).

Section 1. Proteins structure and classification. Database on proteins 3D-structure.

Theme 1. Protein spatial structure prediction by amino acid sequence using comparative modeling method. Modern Internet servers for modeling the 3D proteins structure (5 hours).

Dynamics of molecular systems. Motion equations: Newton`s, Lagrange`s, Hamilton`s. Molecular Dynamics. Numerical integration motion equations. Verlet algorithm (the simplest difference approximation). Jump algorithm (leap-frog algorithm). Verlet speed algorithm.

Active and interactive methods: problem lecture, lecture visualization (4 hours.).

Theme 2. Biomolecules 3D-structure optimization using the Molecular dynamics method (2 hours).

Dynamics of complex systems. Interaction with the environment. Types of molecular ensembles. Influence of the external environment. Thermostats. Temperature. Instant temperature. Equations of molecular system motion, taking into account the presence of a thermostat. Isothermal molecular dynamics (Scaling method). Thermostat Berendsen. Thermostat Nose-Hoover. Stochastic effects of the environment. Brownian dynamics.

Active and interactive methods used: problem lecture, lecture visualization (2 hours).

MODULE III. 3D-structure of biomolecule complexes and its use in biotechnology and molecular pharmacology (6 hours)

Section 1. Modeling of protein-ligand and protein-protein complexes

Theme 1. *Molecular docking with "hard" and "moving" ligand (2 hours).*

Methods for a molecular modeling data analysis. Radial distribution functions. Characteristics of the molecular dynamic trajectories. Oscillation of molecules. Thermodynamic characteristics.

Active and interactive methods used: problem lecture, lecture visualization (2 hours).

Theme 2. Modeling of biological macromolecules, nanostructures, molecules in solution. Search for viral proteins inhibitors using Molecular docking (2 hours)

Protein structures generating using molecular modeling.

Active and interactive methods used: problem lecture, lecture visualization (2 hours).

Theme 3. Oligomeric protein complexes simulation. Molecular docking and ion channel inhibitors (2 hours).

Protein structure generation using molecular mechanics and dynamics.

Active and interactive methods used: problem lecture, lecture visualization (2 hours).

I. PRACTICAL PART OF THE COURSE (36 hours)

Laboratory work 1. Computer modeling in bioorganic chemistry, examples. Introduction to basic program for molecular editing and structure visualization (RASMOL, VEGA ZZ, SPDBV) (6 hours).

1. File formats for describing molecules structure, molecular structure visualization methods, calculating the physicochemical properties of biomolecules.
2. Internet servers for molecule structure modeling and databases for low molecular weight molecules.

Laboratory work 2. Work with modern molecular structure databases: NCBI, PDB, PubChem, CCDC (6 hours).

Laboratory work 3. Comparative modeling of protein structures according to their amino acid sequence. Modeling structures of viral proteins and ion channels (6 hours).

Laboratory work 4. Molecular docking of protein ligand. Docking of viral target proteins with low molecular weight ligands to search for potential inhibitors (6 hours).

Laboratory work 5. Molecular protein-protein docking and docking ion channels/peptides docking, search for potential modulators (6 hours).

Laboratory work 6. Optimization and analysis of the chemical complexes structure using high-performance computing (6 hours).

III. SCHOLASTIC-METHODICAL PROVISIONING FOR THE STUDENTS' INDIVIDUAL WORK

Scholastic-methodical provisioning for the students' individual work in the discipline «Molecular Genetic Technology in Medicine» is presented in Supplement 1 and includes:

- schedule for performing individual work in the discipline, including the approximate time to allocate on each task;
- description of the tasks for individual work of students and methodical recommendations for their completion;
- requirements for submission and registration of results of individual work.

IV. CONTROL FOR ATTAINING THE COURSE GOAL

№	Controled sections/topics of the discipline	Codes and stages of forming the competences		Means for evaluation	
				Current control	Half-way attestation
1	**MODULE I.** Biomolecular modeling and simulation **MODULE II**. Protein structure modeling	GPC-7 - readiness to use main physicochemical, mathematical and other natural science concepts and methods for solving professional problems	Knows	OS-1 Interview	Questions offset 1 semester -1-10
			Is able to	WW1 Test	WW1 Test
			Possesses	OS-3 Report	OS-2 Colloquium
2	**MODULE III**. 3D-structure of biomolecule complexes and its use in biotechnology and molecular pharmacology	PC-2 - ability to conduct preventive medical examinations, clinical examinations and clinical supervision;	Knows	OS-1 Interview	Questions offset 1 semester -11-36
			Is able to	WW1 Test	WW1 Test
			Possesses	OS-3 Report	OS-2 Colloquium
3	**MODULE I**. Biomolecular modeling and simulation **MODULE II.** Protein structure modeling **MODULE III**. 3D-structure of biomolecule complexes and its use in biotechnology and molecular pharmacology	PC-21 - ability to participate in research	Knows	OS-1 Interview	Questions offset 1 semester -1-36
			Is able to	WW1 Test	WW1 Test
			Possesses	OS-3 Report	OS-2 Colloquium
4	**MODULE I**. Biomolecular modeling and simulation **MODULE II.** Protein structure modeling **MODULE III**. 3D-structure of biomolecule	PC-22 - willingness to participate in new methods and techniques implementation aimed at protecting citizens health.	Knows	OS-1 Interview	Questions offset 1 semester -15-30
			Is able to	WW1 Test	WW1 Test

	complexes and its use in biotechnology and molecular pharmacology		Possesses	OS-3 Report	OS-2 Colloquium

Control and methodological materials, as well as criteria and indicators necessary for the assessment of knowledge and skills and characterizing the stages of the competencies formation are presented in Supplement 1.

V. LIST OF EDUCATIONAL LITERATURE AND INFORMATIONAL-METHODICAL REQUIREMENTS FOR THE DISCIPLINE.

Main literature

(electronic and print publications)

1. Genetic Programming / Malcolm I. Heywood, James McDermott, Mauro Castelli, Ernesto Costa, Kevin Sim / Springer International Publishing Switzerland 2016 https://link.springer.com/book/10.1007/978-3-319-30668-1#editorsandaffiliations
2. Cell Reprogramming / Paul J. Verma, Huseyin Sumer / Springer Science+Business Media New York 2015 https://link.springer.com/book/10.1007/978-1-4939-2848-4#editorsandaffiliations

Additional literature (electronic and print)

1. Genetic Programming / Miguel Nicolau, Krzysztof Krawiec, Malcolm I. Heywood, Mauro Castelli, Pablo García-Sánchez, Juan J. Merelo, Victor M. Rivas Santos, Kevin Sim Springer-Verlag Berlin Heidelberg 2014 https://link.springer.com/book/10.1007/978-3-662-44303-3

Online resources and information

1. Informational project “MolBiol” on classical and molecular biology: http://www.molbiol.ru/
2. Bioinformatics portal, programming and data analysis: http://www.bioinformatics.ru/
3. Website of the European Bioinformatics Institute (EMBL-EBI): http://www.ebi.ac.uk/
4. BLAST: Website of computer programs used to search for protein or nucleic acid homologues: http://blast.ncbi.nlm.nih.gov/Blast.cgi
5. GenBank: Database of annotated nucleotide sequences of DNA and RNA: http://www.ncbi.nlm.nih.gov/genbank/

6. UniProt: Annotated protein amino acid sequence database: http://www.uniprot.org/
7. PDB: A database of spatial structures of proteins and nucleic acids: http://www.rcsb.org/pdb/home/home.do
8. SCOPUS: Bibliographic and abstract database of scientific articles: http://www.scopus.com/
9. Web of Science: a search platform that combines abstract databases of publications in scientific journals and patents: https://apps.webofknowledge.com/
10. PubMed: Abstract database of medical and biological publications of the National Center for Biotechnology Information USA (NCBI): http://www.ncbi.nlm.nih.gov/pubmed

LIST OF INFORMATION TECHNOLOGIES AND SOFTWARE

The location of the computer equipment on which the software is installed, the number of jobs	**List of licensed software**
Multimedia auditorium Vladivostok Russian island, Ayaks 10, building 25.1, RM. M723 Area of 80.3 m2 (Room for independent work)	Windows Seven enterprice SP3x64 Operating System Microsoft Office Professional Plus 2010 office suite that includes software for working with various types of documents (texts, spreadsheets, databases, etc.); 7Zip 9.20 - free file archiver with a high degree of data compression; ABBYY FineReader 11 - a program for optical character recognition; Adobe Acrobat XI Pro 11.0.00 - software package for creating and viewing electronic publications in PDF; WinDjView 2.0.2 - a program for recognizing and viewing files with the same format DJV and DjVu.

In order to provide special conditions for the education of persons with disabilities all buildings are equipped with ramps, elevators, lifts, specialized places equipped with toilet rooms, information and navigation support signs

VI. METHODOLOGICAL RECOMMENDATIONS ON THE COMPLETING THE DISCIPLINE

The main source of information and the knowledge-forming component of the discipline "Molecular Genetic Technology in Medicine" is a series of lectures.

Students guidelines:

1. Students must attend all the lectures and note-taking the material presented.
2. The assimilation and consolidation of lecture materials should be carried out in first days after listening to a lecture.
3. First, it is necessary to study the lecture notes, diagrams and figures. If necessary, read to the recommended literature.
4. In conclusion, try to answer the questions of the lecture plan.
5. In case of missing a lecture, study the material on the lecture topic using the recommended literature. This significantly increases self-preparation time.
6. It is necessary to return to the lecture materials again: while preparing for the final lesson; in preparation for the final control (it is necessary to pay attention to the control questions).

Work with educational and scientific literature is the main form of self-preparation work and it is mandatory to pass the oral and test examinations. It includes the development of lecture material, study of recommended sources and literature on the theme of lectures.

The lecture Analytical essay should contain a record of the main questions of the lecture offered by the teacher (when they are shown), the main sources and literature on the topics and conclusions for each question.

An Analytical essay should be made in a separate notebook. It should be neat, readable, and not contain unrelated information or pictures. The Analytical essays of the scientific literature for self-preparation should also be carried out carefully, contain answers to each question posed in the topic, have a link to the source of information, name and year of publication. A synopsis can be a reference (contain only the main key positions), but at the same time allowing to give a complete

answer to the question, it can be detailed. The volume of the Analytical essay is determined by the student.

While working with educational and scientific literature, a student may:

- make notes in the course of reading in the form of a simple or detailed plan (create a list of the main issues discussed in the source);
- to make these (quoting the most important places of the article or monograph, a short summary of the main ideas of the author);
- prepare annotations (a brief summary of the main issues of the work);
- create notes (detailed theses that).

Having chosen the necessary source, one should find the section of interest on the table of contents or the alphabetical index, as well as the section of the lecture notes or textbook of the same name. In case of any difficulties in understanding the educational material, refer to other sources where the presentation may be more accessible.

It should be noted, that working with literature is not only useful as a means of a deeper study of any discipline but also an integral part of the future graduate's professional activity.

One of the forms for self-preparing work with scientific literature is the performance of creative tasks - writing popular science articles, described in detail in Supplement 1.

VII. LOGISTICS DISCIPLINE

For practical work, as well as for the organization of independent work, students have access to the following laboratory equipment and specialized classrooms that meet the current sanitary and fire regulations, as well as safety requirements during training and scientific and industrial works:

Name of the equipped rooms and rooms for independent work	**List of main equipment**
690922, Primorsky Krai, Vladivostok, island Russian, the Saperny Peninsula, the village of ayaks, 10, RM. M820, M823, M826	Laboratory of biomedical cell technologies Device for polymerase chain reaction with the detection of amplification products in" real time " CFX96 Touch Real Time System Camera for electrophoresis Mini-Sub Cell GT System (BioRad 1704467) Camera for vertical electrophoresis Mini-PROTEAN Tetra Cell, BioRad 1658003 Chamber for vertical electrophoresis PROTEAN II xi Cell (BioRad 1651803) System for fixing and processing of electrophoretic gels Gel Fix System Hydrogen index (pH) meter of solutions complete with electrode and calibration system PB-11-P11 A thermostatic shaker ES-20/60 Laboratory centrifuge MiniSpin Autoclavable single-channel HTL dispenser of variable volume 100-1000 µl Discovery Comfort (4046) Autoclavable single-channel HTL dispenser of variable volume 20-200 µl Discovery Comfort (4045) Autoclavable dispenser of odnokon. variable volume 2-20 µl Discovery Comfort (4043) Autoclavable dispenser of odnokon. variable volume 10-100 µl Discovery Comfort (4044) Biacore X100 automated system for the analysis of intermolecular interactions with a set of additional parts and software System for continuous monitoring of living cells in culture, cell-IQ MLF image formation and analysis, Chip Technologies, Czech Republic Personal CO2 incubator - with Galaxy cell monitoring and vitality enhancement system (CO48R-230-1200) Cabinet laminar flow of the 2nd class of biological protection, the size of the working surface 150 cm SafeFAST Elite215S Bactericidal UV air recirculator, UVR-M Magnetic stirrer, MSH-300i Miniracer-shaker MR-1 Thermoshaker tablet, PST-60 HL - 4 System for obtaining ultra-pure water Simplicity (SIMSV00EU) Laboratory centrifuge for sample preparation by centrifugation 5804r

	Refrigerator low-temperature Forma 902 Automatic single-channel variable volume dispenser 0.2-2 µl, Discovery Comfort series (DV2)
Multimedia audience	AIO PC HP ProOne 400 G1 AiO 19.5" Intel Core i3-4130T 4GB DDR3-1600 SODIMM (1x4GB)500GB; Screen projection Projecta Elpro Electrol, 300x173 cm; Multimedia projector, Mitsubishi FD630U, 4000 ANSI Lumen 1920 x 1080; Flush interface with automatic retracting cables TLS TAM 201 Stan; Avervision CP355AF; lavalier Microphone system UHF band Sennheiser EW 122 G3 composed of a wireless microphone and receiver; Codec of videoconferencing LifeSizeExpress 220 - Codeconly - Non-AES; Network camera Multipix MP-HD718; Two 47 " LCD panels, Full HD, LG M4716CCBA; audio commutation and sound amplification Subsystem; centralized uninterruptible power supply
Reading rooms of the Scientific library of the University open access Fund (building a - 10)	Monoblock HP Loope 400 All-in-One 19.5 in (1600x900), Core i3-4150T, 4GB DDR3-1600 (1x4GB), 1TB HDD 7200 SATA, DVD+/-RW,GigEth,wifi,BT,usb kbd/mse,Win7Pro (64-bit)+Win8.1Pro(64-bit),1-1-1 Wty Speed Internet access 500 Mbps. Jobs for people with disabilities equipped with displays and Braille printers.; equipped with: portable reading devices flatbed texts, scanning and reading machines videovelocity with adjustable color spectrums; increasing electronic loops and ultrasonic marker
Accreditation-simulation center of the school of Biomedicine	

Annex 1

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SCHOOL OF BIOMEDICINE

TRAINING AND METHODOLOGICAL SUPPORT INDEPENDENT WORK OF TRAINEES

Molecular Genetic Technology
Educational program
Preparation for 31.05.01. General Medicine
Form of training full-time

Vladivostok
2018

Self-study includes:

1. Library and homework with educational literature and lecture notes;
2. Preparation for practical exercises;
3. Individual task preparation of the essay;
4. Preparation for testing and control interview (offset).

The procedure for the self-study is determined by the schedule for the performance of independent work on the discipline.

The schedule execution of independent work on discipline

№	Date / deadlines	Type of self-preparing work	Estimated time to complete rules	Form of control
1 year of study				
1	1 week	Analytical essay Individual task	2 hrs.	OS-3-Report
2	1-16 week	Presentation on the Analytical essay Presentation of the results of an individual task	12 hrs.	OS-3-Report
3	17-18 week	Preparation for offset/ examination	4 hrs.	OS-1-Interview WW1 - Test

Analytical Essay Topics

On the18 hours discipline of the self-study, within the framework of 1-hour, Analytical essay is carried out on the proposed topics.

1. DNA technology in medical genetics.
2. Achievements of transcriptomics and proteomics in medical genetics. 3. Genetic databases. Database of medical genetics.
3. Mapping and cloning of genes of hereditary diseases. Linkage analysis and genetic mapping Genetic polymorphism.
4. Modern algorithms for prenatal diagnosis of hereditary diseases.
5. Cloning in the study and treatment of human diseases
6. Experimental models in immunogenetics
7. The use of IT in molecular genetics
8. Basics of Cell Biotechnology

9. Insulin and medical biotechnology: diabetes, biosynthesis, products, new types of insulin.
10. Growth hormone and other hormones and medical biotechnologies: human growth hormone, animal growth hormone, fermentation and recovery, other recombinant hormones.
11. Medical biotechnology and hemoglobin, serum albumin and lactoferrin.
12. Medical biotechnology and hemophilia.
13. Medical biotechnologies and anticoagulants and thrombolytic agents: heparin, hirudin, tissue plasminogen activator.
14. Medical biotechnologies and enzyme inhibitors: aprotinin, α1-antitrypsin, glucobay, lipstatin.
15. Medical biotechnologies and tissue reconstruction: traditional approaches, matrix scaffold-guided tissue regeneration, 3D cell cultures, stem cells.
16. Medical biotechnologies and interferons and interleukins: properties and use, cloning and expression, production.
17. Medical biotechnology and erythropoietin: production.
18. Medical biotechnology and tumor necrosis factor.
19. Medical biotechnology and DNAse I.
20. Medical biotechnology and glucocerebrosidase.
21. Medical biotechnologies and vaccines: recombinant vaccines, DNA vaccines.
22. Medical biotechnologies and antibodies: structure, biosynthesis, risks, use, monoclonal antibodies, hybrid technology, production of monoclonal antibodies, use, recombinant and catalytic antibodies.
23. Medical biotechnology and immunoassay: methods.
24. Medical biotechnologies and biosensors: electrochemical biosensors, optical biosensors, natural biosensors.
25. Stem cells and medical biotechnology
26. Basic methods of cell biotechnology

27. Cell Biotechnology in Oncology
28. Cell Biotechnology in Endocrinology
29. Cell Biotechnology in Immunopathology

Guideline for writing and design of the analytical essay

Analytical essay - is an independent educational and research activity, which reproduces in its structure research activities to solve theoretical and applied problems in a particular scientific field. The Analytical essay is a model of scientific research, it is a part of self-study work in which a student solves a theoretical problem, applying the scientific principles and methods. The result of this scientific search can have not only subjective, but also objective scientific novelty, and therefore can be presented for discussion by the scientific community in the form of a scientific report or a message at a scientific-practical conference, as well as a scientific article.

Writing analytical essay means that student should present some argument, and then to analyze it thoroughly. A student doesn't have to summarize facts and things in this analytical work but make an analysis. The supervisor provides advisory assistance and evaluates the process and results of activities. He provides an approximate topic of Analytical essay work, specifies the problem and topic of research with the intern, helps to plan and organize research activities, assigns time and a minimum number of consultations. The supervisor accepts the text of the Analytical essay for verification at least ten days before the defense.

Traditionally there was a certain structure of the Analytical essay, the main elements of which in order of their location are the following:

1. Title page
2. Table of Contents
3. List of symbols, symbols, and terms (if necessary)
4. Introduction
5. The main part
6. Conclusion

7. Bibliographic list
8. Applications

The title page lists educational institution, graduating department, author, scientific advisor, research topic, place and year of the essay. The title of the Analytical essay should be as short as possible and fully consistent with its content. The table of contents (content) reflects the names of the structural parts of an essay and page numbers. The table of contents should be placed at the beginning of the page.

The presence of a detailed introduction - a mandatory requirement for the Analytical Essay. Despite the small volume of this structural part, its writing causes considerable difficulties. However, it is a qualitatively executed introduction that is the key to understanding the entire work, which testifies to the professionalism of the author.

The introduction is a very crucial part of the essay. The introduction should start with a brief justification of the chosen topic. As applied to the analytical essay, the concept of "relevance" has one feature. From how the author of the Analytical essay Is able to choose a topic and how correctly he understands and evaluates this topic from the point of view of modernity and social significance, characterizes his scientific maturity and professional preparedness.

In addition, in the introduction, it is necessary to isolate the methodological basis of the analytical essay, to name the authors, whose works constituted the theoretical basis of the study. A review of the literature on the topic should show the author’s thorough acquaintance with special literature, his ability to systematize sources, critically examine them, highlight the essential, determine the most important parts.

The introduction reflects the importance and relevance of the chosen topic, defines the object and subject, purpose and objectives, and the chronological framework of the study. The introduction ends with a statement of the general conclusions about the scientific and practical significance of the topic, the degree of its knowledge and sources, and the hypothesis being put forward.

The main part describes the essence of the problem, reveals the topic, determines the author's position, factual material is given as an argument and for illustrations of put forward provisions. The author must demonstrate the ability to consistently present the material while analyzing it simultaneously. Preference is given to the main facts, rather than small details.

The Analytical essay ends with the final part, which is called "conclusion". Like any conclusion, this part of the Analytical essay serves as a conclusion, due to the logic of the study, which is a form of synthesis accumulated in the main part of scientific information. This synthesis is a consistent, coherent presentation of the results obtained and their relation to a common goal and specific tasks set and formulated in the introduction. It is here that contains the so-called "output" knowledge, which is new in relation to the original knowledge.

The conclusion may include practical suggestions, thereby increasing the value of theoretical materials. So, in the conclusion of the abstract should be:

a) presents the conclusions of the study;

b) theoretical and practical significance, the relevance of the abstract;

c) indicated the possibility of applying the study results.

After the conclusion, it is acceptable to place the bibliographic list of the used literature. This list is one of the essential parts of the abstract and reflects the independent creative work of the abstract author.

The list of sources is placed at the end of the work. It is made or in alphabetical order (by the name of the author or the name of the book), or in the order in which the references appear in the text of the written work. In all cases, the full title of the work, the names of the authors or the editor of the publication are indicated if the writing team involved a group of authors, data on the number of volumes, the name of the city and publisher in which the work was published, year of publication, number of pages.

Criteria for analytical essay evaluation.

The stated understanding of the abstract as a holistic copyright text defines the criteria for its evaluation: the novelty of the text; the validity of a chosen source; material description rate; matching with the registration requirements.

The novelty of the text:

a) the relevance of the research topic;

b) the novelty and independence in the problem formulation, the formulation of a new aspect of the well-known problem in the establishment of new connections (interdisciplinary, intra-subject, integration);

c) the ability to work with research, critical literature, systematize and structure the material;

d) the appearance of the author's position, independence of assessments and judgments;

d) stylistic unity of the text, the unity of genre features.

Material description rate:

a) the plan complies with the abstract topic;

b) compliance with the content of the topic and plan of the abstract;

c) completeness and depth of knowledge on the topic;

d) the validity of the methods of working with the material;

e) the ability to generalize, draw conclusions, compare different points of view on one issue (problem).

The validity of a chosen source:

a) evaluation of the used literature: whether the most famous works on the topic of research are involved (including recent journal publications, recent statistics, summaries, references, etc.).

Matching with the registration requirements:

a) reference correctness;

b) assessment of literacy and presentation (including spelling, punctuation, stylistic), knowledge of terminology;

c) matching with the requirements for the abstract volume.

The reviewer should clearly state the remark and questions, preferably with references to the work (possible on specific pages of the work), show any evidence that the author did not take into account.

The reviewer can also indicate: whether the student has addressed the topic earlier (essays, written works, creative works, Olympiad works, etc.) and whether there are any preliminary results; how the graduate conducted the work (plan, intermediate stages, consultation, revision and processing of the written or lack of a clear plan, rejection of the recommendations).

The student submits an essay for review no later than a week before the defense (oral presentation). The reviewer is the supervisor. Experience shows that it is advisable to acquaint the student with the review a few days before the defense (oral presentation). Opponents are appointed by the teacher from among the students. For an oral presentation, a student needs about 10–20 minutes.

Grade 5 - if all the requirements for writing and defending an essay are fulfilled: the problem is indicated and its relevance is justified, a brief analysis of different points of view on the problem under consideration is made and one's own position is logically presented, conclusions are formulated, the topic is fully disclosed, the volume is met, external requirements are met design, given the correct answers to additional questions.

Grade 4 - the basic requirements for the abstract and its protection are met, but there are shortcomings. In particular, there are inaccuracies in the presentation of the material; there is no logical sequence in the judgments; not sustained volume of the abstract; there are omissions in the design.

Grade 3 - there are significant deviations from the requirements. In particular, the topic is only partially covered; factual errors occur in abstract text or while answering additional questions.

Grade 2 - the topic of the essay is not disclosed; a significant misunderstanding of the problem is found.

Grade 1 - the student's is not presented.

Annex 2

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SCHOOL OF BIOMEDICINE

FUND ASSESSMENT TOOLS

TRAINING COMPLEX OF DISCIPLINE

Molecular Genetic Technology in Medicine
Educational program
Preparation for 31.05.01. General Medicine
Form of training full-time

Vladivostok
2018

FEA Passport

Completed in accordance with the Regulations on the Funds of Evaluation Assets of Educational Programs of Higher Education - Bachelor's Programs, Specialties, FEFU Magistrates, approved by order of the Rector No. 12-13-850 of 12.05.2015.

Competence code and formulation	**Stages of competence formation**	
GPC-7 - readiness to use main physicochemical, mathematical and other natural science concepts and methods for solving professional problems;	Knows	– place and role of molecular modeling in medicine; – main concepts, definitions, methods and approaches used in molecular genetic studies in medicine; – use of molecular genetic technologies in pharmacology and clinical medicine; – biomedical problems solved by approaches of molecular genetic modeling
	Is able to	– formulate problems of molecular genetic studies in medicine
	Possesses	– the main principles of molecular genetic research organizing in medicine
PC-2 - ability to conduct preventive medical examinations, clinical examinations and clinical supervision;	Knows	– the main principles of medical examinations in order to conduct genetic research
	Is able to	– organize medical examinations in order to conduct genetic research
	Possesses	– the main skills of medical examinations in order to conduct genetic research
PC-21 - ability to participate in research;	Knows	– techniques for molecular genetic studies in medicine
	Is able to	– how to plan molecular genetic studies in medicine;
	Possesses	– skills to plan molecular genetic studies in medicine;
PC-22 - willingness to participate in new methods and techniques implementation aimed at protecting citizens health.	Knows	– methods, technologies and products of molecular genetic studies in medicine
	Is able to	– use knowledge of methods, technologies and products of molecular genetic studies in medicine for the patient treatment
	Possesses	– skills and planning the introduction of new products and molecular genetic studies in medicine for patients treatment

CONTROL FOR ATTAINING THE COURSE GOAL

№ п/п	Controlled sections/topics of the discipline	Codes and stages of forming the competences		Means for evaluation	
				Current control	Half-way attestation
	MODULE I. Biomolecular modeling and simulation **MODULE II.** Protein structure modeling	GPC-7 - readiness to use main physicochemical, mathematical and other natural science concepts and methods for solving professional problems	Knows	OS-1 Interview	Questions offset 1 semester -1-10
			Is able to	WW1 Test	WW1 Test
			Possesses	OS-3 Report	OS-2 Colloquium
	MODULE III. 3D-structure of biomolecule complexes and its use in biotechnology and molecular pharmacology	PC-2 - ability to conduct preventive medical examinations, clinical examinations and clinical supervision;	Knows	OS-1 Interview	Questions offset 1 semester -11-36
			Is able to	WW1 Test	WW1 Test
			Possesses	OS-3 Report	OS-2 Colloquium
	MODULE 1. Biomolecular modeling and simulation **MODULE II.** Protein structure modeling **MODULE III**. 3D-structure of biomolecule complexes and its use in biotechnology and molecular pharmacology	PC-21 - ability to participate in research	Knows	OS-1 Interview	Questions offset 1 semester -1-36
			Is able to	WW1 Test	WW1 Test
			Possesses	OS-3 Report	OS-2 Colloquium
	MODULE 1. Основы компьютерного моделирования биомолекул **MODULE II.** Protein structure modeling **MODULE III**. 3D-structure of biomolecule complexes and its use in	PC-22 - willingness to participate in new methods and techniques implementation aimed at protecting citizens health.	Knows	OS-1 Interview	Questions offset 1 semester -15-30
			Is able to	WW1 Test	WW1 Test

	biotechnology and molecular pharmacology		Possesses	OS-3 Report	OS-2 Colloquium

The scale of assessment the level of formation of competences

Competence code and formulation	Stages of competence formation		Criteria	Indicators	Score
GPC-7 - readiness to use main physicochemical, mathematical and other natural science concepts and methods for solving professional problems	Knows (Minimum level)	• place and role of molecular modeling in medicine; • basic concepts, definitions, methods and approaches used in molecular genetic studies in medicine; • areas of using molecular genetic technologies in pharmacology and clinical medicine; • biomedical problems solved by molecular genetic modeling approaches	• knowledge of the place and role of molecular modeling in medicine; • basic concepts, definitions, methods and approaches used in molecular genetic studies in medicine; • the use of molecular genetic technologies in pharmacology and clinical medicine; • biomedical problems solved by molecular genetic modeling approaches	• formed structured systematic knowledge of the place and role of molecular modeling in medicine; • basic concepts, definitions, methods and approaches used in molecular genetic studies in medicine; • areas of using molecular genetic technologies in pharmacology and clinical medicine; • biomedical problems solved by molecular genetic modeling approaches	65-71
	Is able to (Advance level)	Formulate the tasks of molecular genetic studies in medicine	Skill formulate problems of molecular genetic studies in medicine	Ready and able to formulate the tasks of molecular genetic research in medicine	71-84
	Possesses (Hight level)	The conceptual apparatus, and the basics of organizing molecular genetic research in medicine	Skills of using the conceptual apparatus, and the foundations of the organization of molecular genetic studies in medicine	Systematic application of the conceptual apparatus, and the foundations of the organization of molecular genetic studies in medicine	85-100
PC-2 - ability to conduct preventive medical examinations, clinical examinations and clinical supervision;	Knows (Minimum level)	Fundamentals of the organization of medical examinations in order to conduct genetic research	use knowledge of methods, technologies and products of molecular genetic studies in medicine for the patient treatment	Formed structured systematic knowledge of the organization of medical examinations in order to conduct genetic research	65-71
	Is able to (Advance level)	ability to conduct preventive medical examinations in order to participate in research	ability to organize medical examinations for the purpose of genetic research	ready and able to organize medical examinations for the purpose of conducting genetic research	71-84
	Possesses (Hight level)	Skills of the organization of medical examinations	Skills for organizing medical examinations for	Ability to organize medical examinations for the	85-100

		for the purpose of carrying out genetic researches	the purpose of genetic research	purpose of genetic research	
PC-21 - ability to participate in research	Knows (Minimum level)	Techniques for the formulation and use of technology for molecular genetic studies in medicine	Knowledge of techniques for the formulation and use of technology for carrying out molecular genetic studies in medicine	Formed structured systematic knowledge of techniques for the formulation and use of technology for carrying out molecular genetic studies in medicine	65-71
	Is able to (Advance level)	plan molecular genetic studies in medicine;	Know how to plan molecular genetic studies in medicine	Ready and able to plan molecular genetic studies in medicine	71-84
	Possesses (Hight level)	Skills planning molecular genetic studies in medicine;	Planning Skills for Molecular Genetic Research in Medicine	The ability to confidently plan molecular genetic studies in medicine	85-100
PC-22 - willingness to participate in new methods and techniques implementation aimed at protecting citizens health.	Knows (Minimum level)	Methods, technologies and products of molecular genetic studies in medicine	Knowledge of methods, technologies and products of molecular genetic research in medicine	Formed structured systematic knowledge of methods, technologies and products of molecular genetic research in medicine	
	Is able to (Advance level)	Use knowledge of methods, technologies and products of molecular genetic studies in medicine for the treatment of patients	Ability to use knowledge of methods, technologies and products of molecular genetic studies in medicine for the treatment of patients	Ready and Is able to knowledge of methods, technologies and products of molecular genetic studies in medicine for the treatment of patients	
	Possesses (Hight level)	Skills planning the introduction of products of molecular genetic studies in medicine for the treatment of patients	Skills for planning the introduction of products of molecular genetic studies in medicine for the treatment of patients	The ability to plan the introduction of products of molecular genetic studies in medicine for the treatment of patients	

Guidelines that determine the results of the discipline evaluation procedures development

Current certification of students on the subject «Molecular Genetic Technology in Medicine» is conducted in accordance with the local regulations of the Far Eastern Federal University and is mandatory.

Current certification in the discipline «Molecular Genetic Technology in Medicine» is held in the form of control measures (test papers, tests) on the evaluation of actual student learning outcomes, and by a master teacher.

Examination means of checking the ability to apply this knowledge to solve problems of a certain type on the problems of the course. Complete control tasks in the discipline mainly includes tasks designed to test the knowledge of molecular biology.

Test is a system of standardized tasks to automate the procedure of measuring the level of knowledge and skills of the student. in the discipline Foundation test items include various kinds of tests, such as the establishment of compliance, true / false, the query selects an answer.

The objects of evaluation are:

- Subject matter (the activity in the classroom, the timeliness of the implementation of different types of jobs, the attendance of all classes in the discipline attested);
- The degree of assimilation of theoretical knowledge;
- The level of mastery of practical skills and abilities for all types of academic work;
- The results of independent work.

The interim certification of students on the subject «Molecular Genetic Technology in Medicine» is conducted in accordance with the local regulations of the Far Eastern Federal University and is mandatory.

On the subject «Molecular Genetic Technology in Medicine» is provided offset in the 6 semesters. Test carried out in writing.

Evaluation tools for intermediate certification

Option creative tasks:

1. Draw different conformations of dialanin molecule (different types of α-helix, β-folded sheet, collagen helix) according to the given values of the angles φ, and ω.
2. Calculate the energy of each conformer of the molecule at a given point (without optimizing Calculate> AMMP> Minimization, select Single point). Energy recorded in the table below - in the column Etot (ref). Minimize energy using the Quasi-Newton algorithm in the VegaZZ program, write the energy in the Etot column (finite). Analyze the results. Answer the following questions:

- Which of the original conformer is the most stable?
- In what order does the conformer stability change?
- Which of the final conformers is the most stable? In what order does the stability of the resulting conformers change?
- Does the geometry change much during optimization?
- Is it possible to draw a conclusion regarding how the energy depends on the magnitudes of the angles and the gauche-trans orientation of groups in conformers?

For oral questioning students involves a discussion on the following topic:

1. What modeling methods are used to solve various scientific and practical problems.
2. What is the advantage and limitation of various methods of molecular modeling by force fields?

Option creative tasks:

Read the Roland H. Stote, Martin Karplus article "Zinc Binding in Proteins and A Simple But Accurate Nonbonded Representation" (http://onlinelibrary.wiley.com/doi/10.1002/prot.340230104/Analytical essay) Note the purpose of the study, the method of calculation used and the results of the

study, the method of calculation used and the results of the study. Summarize and briefly outline the content of the article for other students.

Option creative tasks:

Pluronics are polymers consisting of blocks containing polyethylene oxide and polypropylene oxide fragments. A block consisting only of polyethylene oxide fragments is considered hydrophilic, a block of polypropylene oxide fragments is hydrophobic. A combination of these blocks produces amphiphilic molecules that act as surfactants. Using molecular modeling of polymers consisting of (a) polyethylene oxide blocks only, (b) polypropylene oxide blocks only, and (c) block copolymers consisting of 100 polyethylene oxide-100 polypropylene oxide-100 polyethylene oxide blocks, in an aqueous medium, explain:

- Why does such a small variation of the monomer structure lead to a radical change in the hydrophilicity of the polymer?
- What structure do these three polymers form in water?
- The ultimate knowledge control is carried out in the form of an oral test, sample questions for the test are listed below.

Questions for monitoring the survey:

1. What is thermal mobility of atomic systems by the molecular dynamics method? When and for which molecular systems were the first computational experiments conducted using the molecular dynamics method?
2. Give a schematic description of the formulation and conduct of the molecular-dynamic computational experiment.
3. What software systems for modeling molecular dynamics of biomolecular systems are most common at present?
4. 1 kg of water under normal conditions takes up the volume of 1 liter. Find the average volume per water molecule. Estimate the distance between the oxygen of neighboring water molecules, assuming, that water molecules are located at the nodes of a simple cubic lattice.

5. Give the characteristic values of spatial, temporal and energy scales arising from the description of molecular systems. What methods of their assessment can you suggest?
6. 1000 atoms fill the cube and are located at the nodes of a simple cubic lattice. Find the number of atoms (a) lying on the surface of the cube and (b) lying in the surface layer. What percentage of all atoms make up the atoms of these two layers?
7. Give the definition of the calculated cell with periodic boundary conditions. Argue the usefulness of introducing periodic boundary conditions when modeling a condensed state of a substance.
8. Let the condensed molecular system have translational symmetry in three coordinate directions with periods ax, ay, az, respectively. We define the computational cell as a rectangular parallelepiped, which coincides with the periodicity cell and is located at the origin of coordinates. For an arbitrary particle having coordinates (x, y, z), write out formulas (specify an algorithm) for finding the coordinates of its image in the computational cell.
9. A polymer molecule in a dilute solution has a coil state. To model its behavior, a model was proposed in which the polymer was represented by a chain of 100 balls of diameter 1 connected by valence bonds of length 1, and the solvent by simple balls of diameter 1. The calculated cell was taken in the form of a cube with periodic boundary conditions. Estimate the total number of balls that need to be placed in the calculation cell so that in the process of thermal fluctuations of the polymer coil the conditions of the diluted solution are maintained, that is, that the polymer does not have contact with the polymer images in the neighboring cells.
10. The interaction of atoms of neutral gases describes well the potential of Lennard-Jones. Give him a look. Specify the parameters of the potential and their physical meaning. Derive the formulas for the intermolecular interaction forces given by Lennard-Jones potentials.

11. What is the Verlet algorithm is (the simplest difference approximation) for the numerical integration of the classical Newton equations for a system of interacting material particles. How accurate is the atomic coordinates? Prove it! How can one find particle velocities using this method? Specify the accuracy with which there are speeds.
12. Describe the algorithm with jumps (or the leap-frog algorithm) for the numerical integration of the classical equations of motion of interacting atoms. Display calculation formulas. Provide estimates of the accuracy with which coordinates, and velocities are calculated.
13. Provide formulas for the Verlet velocity algorithm for the numerical integration of the classical equations of motion of a molecular system. Show that the trajectory obtained using this method exactly coincides with the trajectories that are given by using the simple Verlet algorithm and the hopping algorithm. What is the advantage of Verlet's high-speed algorithm?
14. Describe the possible ways to bring the simulated molecular system to a state corresponding to a given temperature. Modification of the equations of motion for effective consideration of the thermostatic effect of the external environment.
15. What is "isothermal molecular dynamics"? Write out the equations of motion, which are analogous to Newton's equations, but for which the integral of the equations of motion is not the total energy, but the kinetic energy of the system.
16. Describe the Berendsen thermostat. Write the equations of motion for this case. Note the known disadvantages of using this method for temperature control of the molecular system.
17. Bring the equations of motion of the molecular system using the Nose-Hoover thermostat. Describe what its application is.
18. Describe the formulation of a molecular-dynamic computational experiment to create a cylindrical cavity of a given radius in a phospholipid bilayer.

19. Describe the formulation of a molecular-dynamic computational experiment for the conclusion (compression) of a macromolecule in a cylindrical cavity of a given radius.
20. Describe the possible steps for the preparation and conduct of molecular-dynamic computational experiments of the hydrated phospholipid bilayer with the inclusion of the channel-forming peptide gramicidin A.
21. Construct a potential function describing the interaction of atoms with an impermeable spherocylinder. What might look like a computational experiment on growing a cavity in the shape of a spherocylinder in an already existing model molecular system?

Examples of creative tasks

Task No. 1. Modeling based on the homology of the spatial structure of the transmembrane domain of a potential-dependent potassium channel (pore-forming section).

Introduction. The potential-dependent potassium channel is a homotetramer, each subunit of which contains an electric potential sensor (S1-S4 transmembrane strands) and forming a central pore and filter section (S5-S6). The bacterial homologue of KcsA consists of only two transmembrane domains forming the central pore. 127 Molecular modeling of nano- and biostructures Objective. The transmembrane portions of the channel are underlined, the potential-sensitive segment is italicized. A sequence of two transmembrane α-helices and a P-loop of the HERG receptor is given (see table). For a fragment of the sequence of the channel R534- A671, it is necessary to find structural patterns, build a model of the spatial structure of the protein.

Test questions:

1) How will the absence of S1-S4 transmembrane α-helices affect protein stability?

2) What approximations were made when building the model, how can they affect the results obtained?

3) with the help of what experiments it is possible to confirm or disprove the final model

Task No. 2. Simulation based on the homology of the spatial structure of the mouse transatomonal domain of the melatonin receptor (ML1A_MOUSE).

Introduction. Membrane proteins are very important biological objects, but the determination of their spatial structure using experimental methods is extremely difficult. This is due to the fact that they often cannot be isolated in sufficient quantities to study and are difficult to crystallize. One of the main functions of membrane proteins is receptor: they mediate transmembrane signal transduction through the formation of protein-ligand complexes. Most of the membrane proteins belong to the family of G-protein conjugated receptors (GPCR). They have a common type of folding of the polypeptide chain: 7 transmembrane domains forming a “bundle” of spirals connected by loop regions. In this case, the N-terminus of the protein chain is located in the extracellular region, and the C-terminus is inside the cell. The spectrum of ligands for proteins of this family is extremely wide: they are metal ions, nucleotides, nucleosides, peptides, low-molecular compounds, and even light. For rational design of ligands that selectively and effectively act on the proteins of the GCPR family, it is necessary to have models of their spatial structure. Despite the value of such information, today only the structure of two proteins of this family is known: the visual rhodopsin and adrenergic receptor B2A. These models are widely used as templates for computer modeling of GPSR-receptors based on homology. This approach is proposed to be used to build a model of the three-dimensional structure of the membrane-bound domain of the melatonin receptor - an integral membrane protein from the GPCR family.

Objective: To build a model of the spatial structure of the mouse transfembrane receptor melatonin domain based on homology with bovine rhodopsin. Comparison of the model obtained with the existing human melatonin receptor model. Description: In the process of completing the task, the following steps should be performed:

1. Find in the Swiss-Prot online database (http://www.expasy.org/sprot /) the amino acid sequence of the modeled protein. Extract interesting information

about the sequence (sequencing date, taxonomy of the species, bibliographic references to the object, functions, data on the domain organization). This information should be presented in the report. Save the sequence of the simulated protein in FASTA format.

2. In the database FASTA (http://www.ebi.ac.uk/fasta33/) to find homologues of the modeled protein. Save the sequence of some of them in FASTA format
3. For all stored sequences, construct the multiple alignment and phylogenetic tree using the CLUSTALW tool (http://www.ebi.ac.uk/clustalw/). Based on these data, make a conclusion about the relationship in the family of proteins.
4. Predict the position of transmembrane (TM) sites in the simulated protein by various methods; compare the results. Methods (found on the Internet): HMMTOP, TMHMM, TMPRED, TOP-PRED2.
5. Build a binary (pair-wise) sequence alignment of the simulated protein with the sequence of bovine rhodopsin (opsd_bovin in Swiss-Prot). Discuss alignment with teacher. Refine alignment. Check whether the predicted TM regions of the modeled protein and the experimentally determined rhodopsin match on alignment. Creating a file with instructions for building a model. Building models using the MODELLER program based on the alignment obtained earlier. The choice of the best model based on the analysis of spatial disorders.
6. Optimization of the resulting InsightII molecular shell model: • Addition of hydrogen atoms for physiological PH; • "Step" minimization of the energy of the resulting model: 1) only hydrogen atoms; 2) side chains only; 3) the entire molecule, except for Cα atoms; 4) complete minimization of energy; • Remove loopback sections of the model and capping the resulting structure. 8. Compare the resulting model with the previously constructed ML1A_HUMAN model. 9. According to the results of the work done to write a report.

Test questions:

1. Are there any patterns in the arrangement of conservative and variable (in the melatonin receptor family) amino acid residues of the transmembrane domain?

2. How can we further refine and use the constructed model for the rational design of new ligands - melatonin analogues?

3. What are the sources of possible errors made when creating a model and that can affect its quality?

Control tests

Control tests are designed for students studying the course "Molecular Genetic Technology in Medicine" Tests are necessary both for the control of knowledge in the process of the current intermediate certification, and for the assessment of knowledge, the result of which can be the setting of credit.

When working with tests, the student is invited to choose one option or a combination of answers from the answers given. At the same time, tests are unequal in complexity. Among the proposed there are tests that contain several options for correct answers. The student must specify all the correct answers.

Tests are designed for both individual and collective decision. They can be used in the process and classroom, and independent work. The selection of tests necessary for the control of knowledge in the process of intermediate certification is done by each teacher individually.

The results of the test tasks are assessed by the teacher on a five-point scale for issuing attestation or according to the “test” system - “no test”. The mark "excellent" is set with the correct answer to more than 90% of the tests proposed by the teacher. A rating of "good" - with the correct answer to more than 70% of tests. A rating of "satisfactory" - with the correct answer to 50% of the tests proposed by the student.

Test survey options (test)

TEST 1
MARK ALL RIGHT ANSWER

1. What are pharmacodynamics studies?
   - mechanisms of action of drugs;
   - transformations associated with the biotransformation of drugs, for example, their oxidation;
   - mechanisms of absorption and drugs excretion;
   - patterns of redistribution of drugs in the body.
2. The classical Free-Wilson method assumes:
   - determine the contributions of the biological activity of the substituents;
   - calculation of the conformations of the studied compounds;
   - search for regression dependencies of the structure on physicochemical properties;

   calculation of molecular connectivity indices.

3. Preparations that have a pronounced and specific biological effect:
    - act in low concentrations;
    - have dissociation constants in the range of 10-1 ÷ 10-4 M;
    - have dissociation constants in the range of 10-5 ÷ 10-9 M;
    - have dissociation constants in the range of 10-9 ÷ 10-12 M;
4. The equilibrium dissociation constant is defined as:
    - Kd = [R] [L] / [RL];
    - Kd = [RL] / [R] [L];
    - Kd = kdiss / kass is the quotient from dividing the rate constants of dissociation and association;
    - KD = kdiss kass - product of the rate constants of dissociation and association.
5. The phenomenon of tautomerism:
    - associated with the migration of a mobile group or multiple communication;
    - occurs without breaking the valence bond;
    - is a reversible process;
    - associated with a change in conformation, but not a chemical structure.
6. High complementarity of ligands to receptors suggests:
    - spatial-conformational correspondence of molecules;
    - electrostatic complementarity;
    - compliance of the hydrophobic / hydrophobic groups of the ligand to the receptor;
    - high degree of dependence of activity on optical stereoisomerism.
7. The enthalpy of binding of two molecules is determined by:
    - the ratio of the forces of intermolecular attraction / repulsion;
    - changes in the degree of intramolecular mobility of the interacting molecules;
    - loss of translational or rotational freedom of the molecules forming the complex;
    - release of water molecules and ions.
8. Molecular connectivity indexes:
    - reflect the topological differences in the nature of the compound of atoms in a molecule;
    - describe the conformation of molecules that bind to each other;
    - characterize the physico-chemical properties of the substance;
    - used to search for structure-activity dependencies.
9. Dispersion interactions are determined by:
    - processes of charge transfer between molecules;
    - interaction of ionized fragments;
    - mutual correlations of electron density fluctuations;
    - interaction of permanent dipoles.
10. Protein molecules in biological environment:

- are, as a rule, in the only preferred conformation;
- may have several conformations differing by more than 10 kcal / mol;
- can have many conformations, passing into each other;
- can change their state when associated with elements of the environment.

11. The occurrence of hydrogen bonds:
    - may be associated with proton transfer processes;
    - flows only through the donor mechanism;
    - flows through donor-acceptor mechanism;
    - is a key factor in the occurrence of hydrophobic interactions.

TEST 1

MARK ALL RIGHT ANSWER

1. What are pharmacokinetics studies:
    - mechanisms of action of drugs;
    - dependence time - the concentration of a substance in the test tissue;
    - dose dependence - effect;
    - mechanisms of absorption, distribution, biotransformation and removal of drugs.
2. The classical Hansha method assumes:
    - use of pattern recognition theory;
    - consideration of the values of physical and chemical constants of substituents;
    - determination of the increments of the biological activity of substituents;
    - calculation of the conformations of the studied compounds.
3. The magnitude of the dissociation constant depends on:
    - the dissociation rate constant alone;
    - the ratio of the constants of the rate of association and dissociation;
    - free energy of ligand binding to the receptor;
    - the enthalpy component of the binding energy alone.
4. A high degree of ligand affinity for the receptor, as a rule, is characterized by:
    - values of dissociation constants less than 10-10 M;
    - values of dissociation constants more than 10-6 M;
    - the interaction of hydrophobic surfaces of the ligand and the receptor;
    - interaction of the hydrophilic surfaces of the ligand and the receptor;
5. The entropy of the binding of molecules is determined by:
    - effects of solvation / desolvation of interacting molecules;
    - by electrostatic interaction;
    - changes in the translational, rotational and vibrational freedom of molecules;
    - the degree of conformational mobility of interacting molecules.
6. The occupation theory of Clark receptors suggests that:

- the intensity of the pharmacological response is proportional to the number of receptors employed;
- binding of the first drug molecule affects the attachment of subsequent molecules;
- binding of drugs to the receptor is reversible;
- The binding of drugs to the receptor is non-covalent.

7. The theory of two states of the receptor suggests that:
   - receptors bind ligands only if they are in an unexcited state;
   - receptors can move from the ground state to the excited state only if there is an agonist;
   - there are compounds that have a negative internal activity;
   - In addition to the usual antagonists, there are inverse agonists.
8. Pharmacokinetics studies:
   - kinetics of receptor binding of drugs;
   - biotransformation of medicinal substances;
   - absorption and distribution of drugs;
   - removal of drugs.
9. The degree of absorption of drugs from the gastrointestinal tract is determined by:
   - degree of ionization of drugs, depending on the pH of the medium;
   - suction surface area;
   - binding of drugs with various substances present in the biophase;
   - physical and chemical properties of the drug.
10. The most common method of penetration of drugs is:
    - passive diffusion through the lipid phase of membranes;
    - lightweight transport;
    - active transport;
    - filtration and pinocytosis.
11. The average kinetic energy per degree of freedom under normal conditions is close:
    - 0.3 kcal / mol;
    - 3.0 kcal / mol;
    - 6.0 kcal / mol;
    - 9.0 kcal / mol.
12. The energy of π-cationic interactions is close to the values:
    - 0.1 kcal / mol;
    - 1.0 kcal / mol;
    - 10.0 kcal / mol;
    - 100.0 kcal / mol.

QUESTIONS FOR THE EXAMINATION

1. History of computer modeling; in silico concept. Use of computer methods in biology.
2. The concept of hierarchical organization of macromolecules. Sequence → Structure → Dynamics → Function. MM methods used at each of the listed stages (give examples).
3. The main tasks and concepts of bioinformatics. Examples of existing bioinformational Internet resources.
4. Quantum-mechanical and “classical” approaches to the description of molecular systems. Methods based on the use of empirical force fields (give a brief description).
5. The concept of the conformational space of a polyatomic molecular system. The function of the potential energy of the molecule. Methods for minimizing potential energy - give examples of use for solving problems of physico-chemical biology.
6. Basics of the method of molecular dynamics (MD). Advantages and disadvantages. The concept of the trajectory of MD. Examples of use in the study of biomolecular systems.
7. The use of periodic boundary conditions in MD: the essence of the method, what explains the need for its use?
8. Monte Carlo method. Solving the problem of conformational search using stochastic methods.
9. Basics of the molecular docking method. Algorithms for the search and evaluation of the conformations of the protein-ligand complex. Character solvable with docking tasks.
10. Opportunities and limitations of modern experimental and computer methods for determining the three-dimensional structure of macromolecules.
11. Homology-based modeling. The principle of the method. The choice of the structural template. Evaluation of the quality of the models obtained.

12. Simulation based on homology. An example of the practical use of the method.
13. From theory to practice: the integrated use of MM methods to search for new protein ligands with an unknown three-dimensional structure. Molecular dynamics, its mechanical and ideological foundations.
14. The physical nature of the potentials of molecular interactions and their functional form.
15. Equations of motion of the molecular system. Their difference approximation.
16. Modeling the dynamics of condensed systems. Types of ensembles. Periodic boundary conditions.
17. Verlet algorithm (compiling a list of neighbors) to calculate non-valent interactions.
18. Temperature. Evaluation methods and calculations. Temperature control of the molecular system.
19. Accounting for the solvent. Explicit and implicit solvent accounting.
20. Calculation of pressure in small molecular systems. Barostat Berendsen.
21. Simulation of biological macromolecules. Basics of the approach. Purpose modeling.
22. General scheme of molecular-dynamic computing experiment.
23. Processing of molecular dynamics trajectories. Temporal and spatial autocorrelation functions.
24. Protein as a therapeutic target (TM). Features of the preparation of the structure of the protein to the computational experiment. Protonation of the protein.
25. The value of conformational mobility to determine the state of ionization of protein residues. Estimation of mobility of side radicals.
26. Molecular docking and virtual screening. The main objectives of the method. Diagram of the computational experiment. Analyzing the results and improving the accuracy of molecular docking.

27. Methods for isolating the most important interactions and structural filtering. Fragment docking. Virtual screening of libraries of chemical compounds. The main limitations of the molecular docking method.
28. Model molecular-mechanical potentials. The main types of interactions and their relative energies.