Federal State Autonomous Educational Institution of Higher Education "Moscow Institute of Physics and Technology (National Research University)"

APPROVED
Head of Landau Phystech-School of Physics & Research
A.V. Rogachev

Work program of the course (training module)

course:	Molecular Modelling for Drug Design/Молекулярное моделирование в разработке лекарств
major:	Applied Mathematics and Physics
specialization:	General and Applied Physics/Общая и прикладная физика
	Landau Phystech-School of Physics & Research
	Chair of Biophysics
term:	1
qualification:	Master

Semester, form of interim assessment: 2 (spring) - Exam

Academic hours: 30 AH in total, including:
lectures: 30 AH.
seminars: 0 AH.
laboratory practical: 0 AH.

Independent work: 30 AH.

Exam preparation: 30 AH.

In total: 90 AH, credits in total: 2

Number of course papers, tasks: 2

Author of the program: I.V. Manukhov, doctor of biological sciences

The program was discussed at the Chair of Biophysics 19.06.2023

Annotation

The purpose of the discipline is to familiarize students with the basic concepts and approaches in the field of rational drug design, including gaining skills in working with common databases and formats for presenting information and the structure of chemical compounds, ideas about molecular modeling, docking and other virtual screening approaches, computational approaches for prediction properties of chemical compounds and their biological activity.

1. Study objective

Purpose of the course

To acquaint students with the main concepts and approaches in the field of rational drug design, including gaining skills in working with common databases and formats for presenting information and the structure of chemical compounds, ideas about molecular modeling, docking and other virtual screening approaches, computational approaches for predicting the properties of chemical compounds and their biological activity.

Tasks of the course

1) To develop students' understanding of the main methods and approaches used in the rational development of drugs.

2) Introduce them to common data formats and databases.

3) Develop theoretical knowledge and practical skills in applying the methods of virtual screening of chemical compounds using approaches based on "structure" and "ligand": docking, pharmacophore search, search by similarity.

4) Develop the skills of critical analysis of the literature and the results of computer algorithms, planning and implementing the optimal strategy for rational drug design in real problems.

2. List of the planned results of the course (training module), correlated with the planned results of the mastering the educational program

Mastering the discipline is aimed at the formation of the following competencies:

Code and the name of the competence	Competency indicators
UC-1 Use a systematic approach to critically analyze a problem,and develop an action plan	UC-1.1 Systematically analyze the problem situation, identify its components and the relations between them
	UC-1.2 Search for solutions by using available sources
	UC-1.3 Develop a step-by-step strategy for achieving a goal, foresee the result of each step, evaluate the overall impact on the planned activity and its participants
UC-2 Able to manage the project through all stages of implementation	UC-2.4 Publicly present the project results (or results of its stages) via reports, articles, presentations at scientific conferences, seminars, and similar events
UC-4 Use modern communication tools in the academic and professional fields, including those in a foreign language	UC-4.1 Exchange business information in oral and written forms in Russian and at least one foreign language
	UC-4.2 Use the acquired skills to write, translate, and edit various academic texts (abstracts, essays, reviews, articles, etc.)
UC-6 Determine priorities and ways to improve performance through self-assessment	UC-6.1 Achieve personal growth and professional development, determine priorities and ways to improve performance
	UC-6.2 Evaluate performance results in correlation with the set objectives and applied methods
Gen.Pro.C-1 Gain fundamental scientific knowledge in the field of physical and mathematical sciences	Gen.Pro.C-1.1 Apply fundamental scientific knowledge in the field of physical and mathematical sciences
	Gen.Pro.C-1.2 Consolidate and critically assess professional experience and research findings
Gen.Pro.C-2 Acquire an understanding of current scientific and technological challenges	Gen.Pro.C-2.1 Assess the current state of mathematical research within professional settings
	Gen.Pro.C-2.2 Assess the relevance and practical importance of research in professional settings

in professional settings, and scientifically formulate professional objectives	Gen.Pro.C-2.3 Understand professional terminology used in modern scientific and technical literature and present scientific results in oral and written form within professional communication
Gen.Pro.C-3 Select and/or develop approaches to professional problem-solving with consideration to the limitations and specifics of different solution methods	Gen.Pro.C-3.1 Analyze problems, plan research strategy to achieve solution(s), propose, and combine solution approaches
	Gen.Pro.C-3.2 Employ research methods to solve new problems and apply knowledge from various fields of science (technology)
	Gen.Pro.C-3.3 Gain knowledge of analytical and computational methods of problem-solving, understand the limitations of the implementation of the obtained solutions in practice
Gen.Pro.C-4 Successfully perform a task, analyze the results, and present conclusions, apply knowledge and skills in the field of physical and mathematical sciences and ICTs	Gen.Pro.C-4.1 Apply ICT knowledge and skills to find and study scientific literature and use software products
	Gen.Pro.C-4.3 Justify the chosen method of scientific research
Gen.Pro.C-5 Undertake professional training, achieve professional growth, and become a team leader in a professional sphere, tolerant of social, ethnic, religious, and cultural differences	Gen.Pro.C-5.3 Apply new knowledge and achieve personal and professional growth
Pro.C-1 Assign, formalize, and solve tasks, develop and research mathematical models of the studied phenomena and processes, systematically analyze scientific problems and obtain new scientific results	Pro.C-1.1 Locate, analyze, and summarize information on current research findings within the subject area
	Pro.C-1.2 Make hypotheses, build mathematical models of the studied phenomena and processes, evaluate the quality of the developed model
	Pro.C-1.3 Apply theoretical and/or experimental research methods to a specific scientific task and interpret the obtained results
Pro.C-2 Organize and conduct scientific research and testing independently or as a member (leader) of a small research team	Pro.C-2.1 Plan and conduct scientific research independently or as part of a research team

3. List of the planned results of the course (training module)

As a result of studying the course the student should:

know:

1) a method for extracting and analyzing scientific and technical information of interest on the computer design of drug compounds, computer search and modeling of targets for drug compounds;
2) basic terms and concepts from the field of rational computer design of medicinal compounds and molecular modeling;
3) the main methods and approaches for the search for promising targets for drug compounds, rational computer design of such compounds, as well as evaluation of their physicochemical and ADME profiles by computer methods.

be able to:

1) independently search for specialized literature and choose effective methods of solution according to the applied tasks;
2) use the main methods of computer molecular modeling, computer design, high-performance computer screening to search for new drug compounds;
3) use computer methods to evaluate the physicochemical and ADME profiles of chemical compounds.

master:

1) theoretical material for setting and solving various problems of rational computer design of medicinal compounds and necessary for independent work;
2) computer modeling methods for solving applied problems of rational computer design of medicinal compounds;
3) the skills of collecting, processing and analyzing the necessary information to solve the problem;
4) the main methods of presenting the results obtained in the form of a scientific article, report, presentation or lecture.

4. Content of the course (training module), structured by topics (sections), indicating the number of allocated academic hours and types of training sessions

4.1. The sections of the course (training module) and the complexity of the types of training sessions

№	Topic (section) of the course	Types of training sessions, including independent work			
		Lectures	Seminars	Laboratory practical	Independent work
1	Computer representation of molecular structures and methods for optimizing their geometry, chemical databases	3			3
2	Modeling the structure and dynamics of proteins	3			3
3	Bioinformatics approaches to search for promising drug targets	4			4
4	Molecular docking	4			4
5	Screening of Substances Based on Ligand Information: Pharmacophore Search	4			4
6	High Throughput Virtual Screening of Potential Drugs	4			4
7	Machine Learning for Predicting the Properties and Activity of Chemical Compounds: Building QSAR Models	4			4
8	Application of neural networks for problems of molecular pharmacology	4			4
AH in total		30			30
Exam preparation		30 AH.			
Total complexity		90 AH., credits in total 2			

4.2. Content of the course (training module), structured by topics (sections)

Semester: 2 (Spring)

1. Computer representation of molecular structures and methods for optimizing their geometry, chemical databases

Sources of information about the spatial structure of molecules. Approaches to modeling molecules based on classical and quantum mechanics. Force fields. Optimization of the geometry of molecules, analysis of the conformational space.

2. Modeling the structure and dynamics of proteins

Sources of information about the structure of proteins and protein complexes. Construction of molecular models of proteins de novo and by homology. General ideas about the method of molecular dynamics.

3. Bioinformatics approaches to search for promising drug targets

Analysis of omics data to search for promising protein targets for drugs. Analysis of differential expression of genes and signaling pathways.

4. Molecular docking

The essence of the molecular docking method and its problems. Molecular docking algorithms. Evaluation functions.

5. Screening of Substances Based on Ligand Information: Pharmacophore Search

The concept of pharmacophore. Methods of combination of molecules.

6. High Throughput Virtual Screening of Potential Drugs

Preparation of compound libraries for virtual screening. Filtering virtual screening results.

7. Machine Learning for Predicting the Properties and Activity of Chemical Compounds: Building QSAR Models

The essence of QSAR. Direct and inverse problems. molecular descriptors. Reliability of QSAR models.

8. Application of neural networks for problems of molecular pharmacology

General overview of machine learning and artificial intelligence methods. Approaches to the representation of the structure of molecules, fingerprints. Application of neural networks to predict the physicochemical and ADME properties of molecules. Examples of using generative networks (GANs) to generate new connections with desired properties.

5. Description of the material and technical facilities that are necessary for the implementation of the educational process of the course (training module)

Classroom with a media projector and screen, Internet access.

6. List of the main and additional literature, that is necessary for the course (training module) mastering

Main literature

Фонд базовой кафедры:

1. Молекулярное моделирование : теория и практика / Х.-Д. Хёльтье, В. Зиппль, Д. Роньян, Г. Фолькерс . — Москва, Лаборатория знаний, 2020.— URL: http://books.mipt.ru/book/301428 (дата обращения: 25.02.2021). - Полный текст (Режим доступа : из сети МФТИ / Удаленный доступ)
2. Neil C. Jones, Pavel A. Pevzner, An Introduction to Bioinformatics Algorithms, MIT Press, 2004.

Additional literature

Фонд базовой кафедры:

1. Young, D.C. Computational drug design: a guide for computational and medicinal chemists / D.C. Young. – N.Y. : Wiley, 2009. – 344 p.

7. List of web resources that are necessary for the course (training module) mastering

Открытые базы данных химической и медико-биологической информации (Chembl, drugbank, gencards, pubmed, GEO)

8. List of information technologies used for implementation of the educational process, including a list of software and information reference systems (if necessary)

Not used

9. Guidelines for students to master the course

A student studying the discipline must, on the one hand, master the general conceptual apparatus, and on the other hand, must learn to apply theoretical knowledge in practice.

As a result of studying the discipline, the student must know the basic definitions and concepts, be able to apply the knowledge gained to solve various problems.

Successful completion of the course requires:

- attendance of all classes provided for by the curriculum for the discipline;
- keeping a synopsis of classes;
- student's intense independent work.

Independent work includes:

- reading recommended literature;
- study of educational material, preparation of answers to questions intended for independent study;
- solving problems offered to students in the classroom;
- preparation for the performance of tasks of the current and intermediate certification.

An indicator of mastery of the material is the ability to answer questions on the topics of the discipline without a synopsis.

It is important to achieve an understanding of the material being studied, not its mechanical memorization. If a student finds it difficult to study certain topics, questions, he/she should seek advice from a teacher.

Intermediate control of students' knowledge is possible in the form of solving problems in accordance with the topic of classes.

SUPPLEMENT

Assessment funds for course (training module)

major:	Applied Mathematics and Physics
specialization:	General and Applied Physics/Общая и прикладная физика Landau Phystech-School of Physics & Research Chair of Biophysics
term:	1
qualification:	Master

Semester, form of interim assessment: 2 (spring) - Exam

Author: I.V. Manukhov, doctor of biological sciences

1. Competencies formed during the process of studying the course

Code and the name of the competence	Competency indicators
UC-1 Use a systematic approach to critically analyze a problem,and develop an action plan	UC-1.1 Systematically analyze the problem situation, identify its components and the relations between them
	UC-1.2 Search for solutions by using available sources
	UC-1.3 Develop a step-by-step strategy for achieving a goal, foresee the result of each step, evaluate the overall impact on the planned activity and its participants
UC-2 Able to manage the project through all stages of implementation	UC-2.4 Publicly present the project results (or results of its stages) via reports, articles, presentations at scientific conferences, seminars, and similar events
UC-4 Use modern communication tools in the academic and professional fields, including those in a foreign language	UC-4.1 Exchange business information in oral and written forms in Russian and at least one foreign language
	UC-4.2 Use the acquired skills to write, translate, and edit various academic texts (abstracts, essays, reviews, articles, etc.)
UC-6 Determine priorities and ways to improve performance through self-assessment	UC-6.1 Achieve personal growth and professional development, determine priorities and ways to improve performance
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	Gen.Pro.C-4.3 Justify the chosen method of scientific research
Gen.Pro.C-5 Undertake professional training, achieve professional growth, and become a team leader in a professional sphere, tolerant of social, ethnic, religious, and cultural differences	Gen.Pro.C-5.3 Apply new knowledge and achieve personal and professional growth
Pro.C-1 Assign, formalize, and solve tasks, develop and research mathematical models of the studied phenomena and processes, systematically analyze scientific problems and	Pro.C-1.1 Locate, analyze, and summarize information on current research findings within the subject area
	Pro.C-1.2 Make hypotheses, build mathematical models of the studied phenomena and processes, evaluate the quality of the developed model

systematically analyze scientific problems and obtain new scientific results	Pro.C-1.3 Apply theoretical and/or experimental research methods to a specific scientific task and interpret the obtained results
Pro.C-2 Organize and conduct scientific research and testing independently or as a member (leader) of a small research team	Pro.C-2.1 Plan and conduct scientific research independently or as part of a research team

2. Competency assessment indicators

As a result of studying the course the student should:

know:

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be able to:

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3) the skills of collecting, processing and analyzing the necessary information to solve the problem;
4) the main methods of presenting the results obtained in the form of a scientific article, report, presentation or lecture.

3. List of typical control tasks used to evaluate knowledge and skills

In order to control the students' mastery of the training material, an oral questioning is conducted at the beginning of the lesson on the topic of the last session.

4. Evaluation criteria

Checking questions:

1. Common databases used in chemo- and bioinformatics.
2. Molecular representations: descriptors and fingerprints.
3. Molecular docking. Structure of force fields and energy functions used in molecular docking.
4. Pharmacophores and pharmacophore search.
5. Molecular descriptors and filters. Common filters for selecting "drug-like" compounds (rule 5, etc.).
6. Models for searching for regularities structure-property and structure-activity (QSAR). Common approaches for building such models.
7. Deep learning methods in drug development. Basic approaches and perspectives.
8. What quantities are used to quantify the interaction between a biological target and a ligand? How do they compare?
9. Types of intermolecular interactions important for the formation of protein-ligand complexes. Their characteristic energy contributions.
10. Basic strategies for computer-aided drug design.
11. Kinetics and thermodynamics of the interaction of ligands with targets. Types of inhibition. Kd and IC50.

12. Approaches for the search for biological targets.
13. Main types of representation of data on the structures of molecules. Common formats.

Examples of exam question papers:
Question paper 1.
1. What quantities are used to quantify the interaction between a biological target and a ligand? How do they compare?
2. Types of intermolecular interactions important for the formation of protein-ligand complexes. Their characteristic energy contributions.
Question paper 2.
1. Approaches for the search for biological targets.
2. Main types of representation of data on the structures of molecules. Common formats.
Question paper 3.
1. Basic strategies for computer-aided drug design.
2. Kinetics and thermodynamics of the interaction of ligands with targets. Types of inhibition. Kd and IC50.
Question paper 4.
1. Common databases used in chemo- and bioinformatics.
2. Molecular representations: descriptors and fingerprints.
Question paper 5.
1. Molecular docking. Structure of force fields and energy functions used in molecular docking.
2. Pharmacophores and pharmacophore search.

Assessment “excellent (10)” is given to a student who has displayed comprehensive, systematic and deep knowledge of the educational program material, has independently performed all the tasks stipulated by the program, has deeply studied the basic and additional literature recommended by the program, has been actively working in the classroom, and understands the basic scientific concepts on studied discipline, who showed creativity and scientific approach in understanding and presenting educational program material, whose answer is characterized by using rich and adequate terms, and by the consistent and logical presentation of the material;

Assessment “excellent (9)” is given to a student who has displayed comprehensive, systematic knowledge of the educational program material, has independently performed all the tasks provided by the program, has deeply mastered the basic literature and is familiar with the additional literature recommended by the program, has been actively working in the classroom, has shown the systematic nature of knowledge on discipline sufficient for further study, as well as the ability to amplify it on one’s own, whose answer is distinguished by the accuracy of the terms used, and the presentation of the material in it is consistent and logical;

Assessment “excellent (8)” is given to a student who has displayed complete knowledge of the educational program material, does not allow significant inaccuracies in his answer, has independently performed all the tasks stipulated by the program, studied the basic literature recommended by the program, worked actively in the classroom, showed systematic character of his knowledge of the discipline, which is sufficient for further study, as well as the ability to amplify it on his own;

Assessment “good (7)” is given to a student who has displayed a sufficiently complete knowledge of the educational program material, does not allow significant inaccuracies in the answer, has independently performed all the tasks provided by the program, studied the basic literature recommended by the program, worked actively in the classroom, showed systematic character of his knowledge of the discipline, which is sufficient for further study, as well as the ability to amplify it on his own;

Assessment “good (6)” is given to a student who has displayed a sufficiently complete knowledge of the educational program material, does not allow significant inaccuracies in his answer, has independently carried out the main tasks stipulated by the program, studied the basic literature recommended by the program, showed systematic character of his knowledge of the discipline, which is sufficient for further study;

Assessment “good (5)” is given to a student who has displayed knowledge of the basic educational program material in the amount necessary for further study and future work in the profession, who while not being sufficiently active in the classroom, has nevertheless independently carried out the main tasks stipulated by the program, mastered the basic literature recommended by the program, made some errors in their implementation and in his answer during the test, but has the necessary knowledge for correcting these errors by himself;

Assessment “satisfactory (4)” is given to a student who has discovered knowledge of the basic educational program material in the amount necessary for further study and future work in the profession, who while not being sufficiently active in the classroom, has nevertheless independently carried out the main tasks stipulated by the program, learned the main literature but allowed some errors in their implementation and in his answer during the test, but has the necessary knowledge for correcting these errors under the guidance of a teacher;

Assessment “satisfactory (3)” is given to a student who has displayed knowledge of the basic educational program material in the amount necessary for further study and future work in the profession, not showed activity in the classroom, independently fulfilled the main tasks envisaged by the program, but allowed errors in their implementation and in the answer during the test, but possessing necessary knowledge for elimination under the guidance of the teacher of the most essential errors;

Assessment “unsatisfactory (2)” is given to a student who showed gaps in knowledge or lack of knowledge on a significant part of the basic educational program material, who has not performed independently the main tasks demanded by the program, made fundamental errors in the fulfillment of the tasks stipulated by the program, who is not able to continue his studies or start professional activities without additional training in the discipline in question;

Assessment “unsatisfactory (1)” is given to a student when there is no answer (refusal to answer), or when the submitted answer does not correspond at all to the essence of the questions contained in the task.

5. Methodological materials defining the procedures for the assessment of knowledge, skills, abilities and/or experience

The course is graded at an exam. The questioning starts with a random task assigned to each student and time given for completion of the task. No aids are allowed. The student then proceeds to a chat with the examiner, at which he/she presents his/her solution to the assigned task. The examiner then asks the student several questions that evenly cover the course content. A final grade is assigned based on the quality of answers and demonstrated level of understanding.