BIOINFORMATICS EDUCATION IN THE INSTITUTE OF BIOMEDICAL CHEMISTRY RAMS:
COURSE «BIOINFORMATICS – THE WAY FROM GENE TO DRUG» AND SPECIAL COURSE «BIOINFORMATICS AND COMPUTER-AIDED DRUG DESIGN»

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SUMMARY

Motivation: Last years the genomics and proteomics discovery lead to extremely fast growth of information in molecular biology area. As bioinformatics becomes integral to biomedical research, there is a need of reorganization of education process in biomedical high schools by introducing bioinformatics theoretical and training courses.

Results: Described bioinformatics education is an example of integration of the higher school (Russian State Medical University, Medico-Biological Faculty) and academic science (Institute of Biomedical Chemistry RAMS). Education consists of theoretical course “Bioinformatics – the way from gene to drug” targeted for students on their 8th semester and special course “Bioinformatics and computer-aided drug design” for students on 11th semester. The last one includes theoretical study (lectures and seminars) and practical training in computer classroom as well as in laboratories of Bioinformatics Department of the Institute of Biomedical Chemistry RAMS.

Availability: All students from biomedical high schools as well as postgraduate students are welcome to our course “Bioinformatics – the way from gene to drug” which is giving since 2000 and special course “Bioinformatics and computer-aided drug design” which is giving since 1995. Lectures and seminars presentations (pdf format) are available on request from the authors.

INTRODUCTION

The fast growth of genomic and proteomic researches has led to multiple increase of our knowledge and explosive development of bioinformatics technologies, which become now an integral discipline in biomedical science. This situation generates the need of reorganization of education process in biomedical high schools by introducing bioinformatics theoretical and training courses.

Described bioinformatics courses are an example of integration of higher school (Russian State Medical University, Medico-Biological Faculty) and academic science (Institute of Biomedical Chemistry RAMS).

Students study algorithms and principles of applied programs for analysis of primary, secondary and tertiary structure of proteins; designing small ligands and simulation of their interaction with biological macromolecules; prediction of pharmacological properties of new substances; molecular modeling, molecular docking, database mining
and de novo design. Practical training is carried out in well-equipped computer classroom and in laboratories of the Institute of Biomedical Chemistry RAMS.

Bioinformatics education consists of theoretical course “Bioinformatics – the way from gene to drug” targeted for students (biophysics, biochemistry and medical cybernetics) on their 8th semester and special course “Bioinformatics and computer-aided drug design” for students on 11th semester of Medico-Biological Faculty of Russian State Medical University.

**METHODOLOGY**

Bioinformatics teaching is based on combination of traditional and modern approaches: giving lectures with using of computer presentations in PowerPoint program, seminars using direct access to the Internet bioinformatics resources, practical training and exercises at computer classroom, real scientific works in research laboratories, intermediate written tests and semester final examination.

*Available hardware:* SGI servers Origin-350 (8 CPU), 3 servers SGI Origin-200 (2 CPU), Linux cluster (32 CPU), 3 workstation SGI O2 and about 40 PCs.

*Available software:* molecular modeling suits Sybyl (Tripos Inc.), Amber, Gromacs, PASS, DockSearch, some academic programs, free software, etc.

**IMPLEMENTATION**

The main focus of our bioinformatics courses lies in the set of topics, which brief review is given below.

1. Bioinformatics: definition, purposes, tasks and place in modern biomedical science.
   - **Bioinformatics unites genomics and proteomics with classical disciplines (molecular biology, biochemistry, biophysics, molecular pharmacology).**
   - **Introduction in bioinformatics, the review of the basic purposes and problems.**

2. Integral platform “From gene to drug” in silico and in vitro (Ivanov, 2005).
   - **Bioinformatics technologies in the integrated platform “From genome to drug”.**
   - **Search of new potential target proteins and experimental validation.**
   - **Experimental analysis and computer 3D modeling of target proteins.**
   - **Search and design new ligands based on 3D structure of target protein.**
   - **Prediction of lead compounds activity and in vitro testing.**

3. Basic principles of computer molecular modeling (Ivanov et al., 2005).
   - **Computational chemistry, methods and approaches.**
   - **Computer modeling of proteins 3D structures and their complexes.**
   - **Molecular mechanics (force fields, parameterization, energy minimization, conformation analysis, molecular dynamics simulation).**
   - **Quantum mechanics (ab initio and semi-empirical approaches).**

4. Analysis of biological texts.
   - **Software for storage, processing and analysis of biological texts.**
   - **Methods of sequence alignment of biopolymers.**
   - **Analysis of structure-functional similarity of new proteins.**
   - **Multiple alignment, patterns, motives and domains, proteins families.**
   - **Bioinformatics approaches in creation of new generation vaccines.**

5. Comparative genome analysis and search of new molecular targets.
   - **Comparative genomics and computer design of new antibacterial drugs.**
   - **Choice of new target in drug discovery pipeline.**
   - **Requirements to the new target proteins and criteria of choice.**
   - **Automated targets search: programs CATS, GenMesh.**
• An example of new targets search for creation of new antituberculosis drugs.
• Further use of potential targets list.
• Protein function prediction at high and low homology with known proteins.

6. Proteins superfamilies, Cytochrome P450 Database (CPD).
• Proteins superfamilies.
• Proteins superfamily formation, structural similarity and functions variety of superfamily members.
• Software for comparative analysis and classification of proteins in superfamily.
• Cytochromes P450 – from superfamily formation to computer modeling and planning of genetic engineering experiments.

• Tasks, problems and approaches of bioinformatics in genome data analysis.
• Known full genomes: current situation, databases.
• Full genome annotation.

• Proteins inventory.
• Proteomics methods: 1D and 2D electrophoreses, HPLC, mass-spectrometry, bioinformatics.
• Protein identification using proteins separation and mass-spectrometry analysis.
• The modern bioinformatics approaches in applied proteomics.
• Review of programs for the of 2D-electrophoresis image analysis, databases.
• Algorithms of protein sequence identification based on peptides mass-spectra.

9. Methods of analysis of protein 3D structures, database PDB.
• Methods of analysis of protein 3D structures, problems and prospects of structural molecular biology.
• Proteins x-ray crystallography, problems of proteins crystallization.
• NMR spectroscopy - physical bases, NMR analysis of protein structure.
• Various types of microscopy.
• Protein Data Bank (PDB).

• Homology modeling of protein 3D structure.
• Modeling of cytochromes P450 (Ivanov et al., 2003).

11. Proteins – molecular targets for drugs.
• Review of structures of known target proteins.
• Searching of new targets.
• Targets for creation of drugs against HIV.
• Protein-protein interactions – new targets (Veselovsky, 2002).

• Transformation of casual drug search into the rational drug design.
• Computer methods in early stages of new drug search.
• Review of computer technologies application in drug discovery.

• Role and place of computer drug design in classical scheme of drug creation.
• Dogma of modern molecular pharmacology.
• The basic stages of structure-based drug design.
• Integration of computer and experimental methods in the way from gene to drug.

• Algorithms of molecular docking.
• Programs DOCK, AUTODOCK and LEAPFROG.
• Using of molecular docking for modeling and lead search.
• Program DockSearch, integration with Sybyl.
• Searchig of cytochromes P450 ligands.
15. Inhibitors of protein-protein interactions and protein dimerization.
   - Strategy of design of protein-protein interaction inhibitors.
   - Inhibitors of HIV protease dimerization.
16. Quantitative structure-property relationship (QSAR), lead search and optimization.
   - Structure-activity relationship, QSAR.
   - Ligand-based drug design.
   - Known drugs designed with using computer technologies.
17. Prediction of biological activity spectra, creation of more safety and effective drugs.
   - Prediction of biological activity spectrum using compound structural formula.
   - Computer program PASS.

DISCUSSION

Described bioinformatics courses can be useful for any students and post-graduates wishing to learn the bases of computer biochemistry, biophysics and pharmacology.

From 1995 this courses were passed by > 500 students (biochemists, biophysics, medical cybernetics) from Russian State Medical University, about 30 students from Sechenov Moscow Medical Academy (pharmacists), from Moscow Institute of Engineering and Physics (cybernetic), from Moscow Physics-technical Institute (biophysics), post-graduates from RAMS, as well as employees from the Institute of Biomedical Chemistry and the Institute of Pharmacology RAMS.

The best graduates of these courses made their diploma in the Institute of Biomedical Chemistry RAMS and later PhD dissertation as RAMS postgraduate.

REFERENCES