

GENERAL INFORMATION

1. NAME OF THE CENTER AND LOCATION

Institute of Biophysics and Biomedical Engineering – Bulgarian Academy of Sciences (IBPhBME – BAS)

Acad. Georgi Bonchev Str., Block 21, Sofia 1113, Bulgaria

2. TYPE OF THE RESEARCH INFRASTRUCTURE AND/OR SCIENTIFIC EXPERTISE

Identify the type of the RI, equipment/facilities/specific research, and in particular linked to COVID-19:

The main directions of research of IBPhBME – BAS are:

- Investigation on the structure-functional relations between lipids and proteins in biological membranes;
- Electroinduced and photoinduced events in cells;
- Bioelectrical processes in excitable cells;
- Elucidation of the mechanisms underlying membrane-associated pathological processes;
- Modelling of lipid-protein, pigment-lipid and cellular interactions by model lipid membranes, biophysical molecular and mathematical models;
- Development of methods and tools for registration, processing and analysis of electrophysiological signals;
- Motor control and biomechanics;
- Development of algorithms, software and hardware devices for medicine;
- Application of information technologies in healthcare;
- *In silico* study of bioactive molecules including QSAR and molecular modeling for estimation of their biological effects.

With the expertise in the field of *in silico* evaluation of biologically active molecules, IBPhBME – BAS could support targeted search for substances with potential effects against COVID-19.

Scientific equipment for biomedical and pharmaceutical research & development available at IBPhBME – BAS includes has a variety of scientific equipment, among them: spectrophotometers, spectrofluorometers, gas chromatograph, scintillation counter, luminometer, ultracentrifuge, computerized system for microscopic image analysis and processing, patch clamp, set-up for high-sensitivity differential scanning microcalorimetry, differential scanning densitometer, cell culture laboratory, electromyograph, electroencephalograph, computerized stations for

analysis of signals from different electrocardiographic leads' systems, set-up for microelectrode investigations, automated system for electrophysiological and biomechanical studies, system for high performance liquid chromatography determination of amino acids after in vivo brain micro dialysis, isometric force measurements in resistant blood vessels (Mulvany's myography), polarographic oxygen rate electrode, microplate reader, inverted fluorescent microscope.

KEY WORDS: biophysics, biomedical engineering, bioinformatics, *in silico* drug design.

3. TYPE OF THE RESEARCH

Provide information on the research carried on or planned in regard with COVID-19 and other viruses

Regarding the expertise in the field of computer-aided drug design, scientists from IBPhBME – BAS have the opportunity to pursue approaches to redirect existing drugs for the treatment of other diseases (*repurposing old drugs*) and to search for new target biomacromolecules (*target fishing*) of existing drugs as well as of naturally occurring compounds used in practice. Related to the above two approaches is the search for multitarget drugs that could bind to more than one target protein. The proposed approaches are in accordance to the World Health Organization directives that aim at implementing computer-aided approaches to accelerate the evaluation of new therapeutics and vaccines.

For the experimental validation of the *in silico* results, IBPhBME can rely on the research expertise and facilities of scientific teams from the other institutes of the Bulgarian Academy of Sciences, e.g. the Institute of Molecular Biology "Roumen Tsanev", The Stephan Angeloff Institute of Microbiology, The Institute of Experimental Morphology, Pathology and Anthropology with Museum, etc. IBPhBME can also collaborate with international research groups, with which the scientists from IBPhBME – BAS have a long-standing fruitful cooperation.

4. WEBSITE

Provide the internet address:

<http://biomed.bas.bg/en/>

5. BACKGROUND, PUBLICATIONS AND OPEN DATA REPOSITORY

leading research team AND Scientific

Leading research team is the core of the QSAR and Molecular Modelling Department (<http://biomed.bas.bg/en/departments/qsar-and-molecular-modelling/>):

publications of the research group on the topics of related to coronaviruses research results;

link to open data repository

- [Prof. Ilza Pajeva, DSc.](#), Head of Department
- [Prof. Tania Pencheva, PhD](#)
- [Assoc. Prof. Ivanka Tsakovska, PhD](#)
- [Senior Assist. Prof. Merilin Al Sharif, PhD](#)
- [Petko Alov, specialist](#)

Selected publications from the last 5 years (in bold are the names of the QSAR and Molecular Modelling Department members):

1. **Alov, P., Tsakovska, I., Pajeva, I.** Computational Studies of Free Radical-Scavenging Properties of Phenolic Compounds. *Current Topics in Medicinal Chemistry*, 15, 2, **2015**, 85-104.
2. Burton, J., Worth, A.P., **Tsakovska, I., Diukendjieva, A.** *In silico* Models for Acute Systemic Toxicity, In: *In silico* Methods for Predicting Drug Toxicity. *Methods in Molecular Biology*, Benfenati E (Ed.), 1425, **2016**, 177-200.
3. **Al Sharif, M., Alov, P., Diukendjieva, A., Vitcheva, V., Simeonova, R., Krasteva, I., Shkondrov, A., Tsakovska, I., Pajeva, I.** Molecular determinants of PPAR γ partial agonism and related *in silico* / *in vivo* studies of natural saponins as potential type 2 diabetes modulators. *Food Chem Toxicol*, 112, **2017**, 47-59.
4. **Al Sharif, M., Alov, P., Vitcheva, V., Diukendjieva, A., Mori, M., Botta, B., Tsakovska, I., Pajeva, I.** Natural modulators of nonalcoholic fatty liver disease: Mode of action analysis and *in silico* ADME-Tox prediction. *Toxicol Appl Pharmacol*, 337, **2017**, 45-66.
5. **Al Sharif, M., Tsakovska, I., Pajeva, I., Alov, P.,** Fioravanzo, E., Bassan, A., Kovarich, S., Yang, C., Mostrag-Szlichtyng, A., Vitcheva, V., Worth, A.P., Richarz, A.N., Cronin, M.T.D. The application of molecular modelling in the safety assessment of chemicals: A case study on ligand-dependent PPAR γ dysregulation. *Toxicology*, 392, **2017**, 140-154.
6. **Diukendjieva, A., Al Sharif, M., Alov, P., Pencheva, T., Tsakovska, I., Paeva, I.** ADME/Tox Properties and Biochemical interactions of Silybin Congeners: *In silico* Study. *Natural Product Communications*, 12, 2, **2017**, 175-178.
7. **Jereva, D., Fratev, F., Tsakovska, I., Alov, P., Pencheva, T., Pajeva, I.** Molecular Dynamics Simulation of the Human Estrogen Receptor Alpha: Contribution to the Pharmacophore of the Agonists. *Mathematics and Computers in Simulation*, **2017**, 124-134.
8. **Tsakovska, I., Pajeva, I., Al Sharif, M., Alov, P.,** Fioravanzo, E., Kovarich, S., Worth, A.P., Richarz, A.-N., Yang, C., Mostrag-Szlichtyng, A., Cronin, M.T.D. Quantitative structure-skin permeability relationships. *Toxicology*, 387, **2017**, 27-42.
9. Angelova, V., Voinikov, Y., Andreeva-Gateva, P., Surcheva, S., Vassilev, N., **Pencheva, T.,** Tchekalarova, J. *In vitro* and *in silico* Evaluation of Chromene Based Aroyl Hydrazones as Anticonvulsant Agents. *Medicinal Chemistry Research*, 26, 9, **2017**, 1884-1896.

10. Labbé, C., **Pencheva, T., Jereva, D.**, Desvillechabrol, D., Becot, J., Villoutreix, B., **Pajeva, I.**, Miteva, M. AMMOS2: A Web Server for Protein-ligand-water Complexes Refinement via Molecular Mechanics. *Nucleic Acids Research*, 45(W1), **2017**, W350-W355.
 11. Stoyanova, T., **Lessigiarska, I.**, Mikov, M., **Pajeva, I.**, Yanev, S. Xanthates as useful probes for testing the active sites of Cytochromes P450 4A11 and 2E1. *Frontiers in Pharmacology*, 8, **2017**, Article 67.
 12. Angelova, V., Valcheva, V., **Pencheva, T.**, Voynikov, Y., Vassilev, N., Mihaylova, R., Momekov, G., Shivachev, B. Synthesis, Antimycobacterial Activity and Docking Study of 2-aryl-[[1]benzopyrano[[4,3-c]]pyrazol-4(1H)-one Derivatives and Related Hydrazide-hydrazones. *Bioorganic & Medicinal Chemistry Letters*, 27, 13, **2017**, 2996-3002.
 13. Angelova, VT; Voynikov, Y; Andreeva-Gateva, P ; Surcheva, S; Vassilev, N; **Pencheva, T**; Tchekalarova, J. In vitro and in silico evaluation of chromene based aryl hydrazones as anticonvulsant agents. *Medicinal Chemistry Research*, **2017**, 26 (9), 1884-1896
 14. **Al Sharif M., A. Diukendjieva-Todorova, P. Alov, V. Vitcheva, M. Mori, B. Botta, I. Tsakovska, I. Pajeva.** Natural modulators of nonalcoholic fatty liver disease: mode of action analysis and in silico ADMET prediction, *Toxicology and Applied Pharmacology*, **2017**, 337, 45-66.
 15. **Al Sharif M., P. Alov, A. Diukendjieva,** Vitcheva; R. Simeonova, I. Krasteva, A. Shkondrov, **I. Tsakovska, I. Pajeva.** Molecular determinants of PPAR γ partial agonism and related in silico / in vivo studies of natural saponins as potential type 2 diabetes modulators, *Food and Chemical Toxicology*, **2018**, 112, 47-59.
 16. **Diukendjieva, A., P. Alov, I. Tsakovska, T. Pencheva,** Richarz, V. Kren, M.T.D. Cronin, **I. Pajeva.** In vitro and in silico studies of the membrane permeability of natural flavonoids from *Silybum marianum* (L.) Gaertn. and their derivatives, *Phytomedicine*, **2019**, 53, 79-85.
 17. **Al Sharif, M., V. Vitcheva, R. Simeonova, I. Krasteva, V. Manov, P. Alov, G. Popov, A. Shkondrov, I. Pajeva.** In silico and in vivo studies of Astragalus glycyphylloides saponin(s) with potential relevance to metabolic syndrome modulation, *Food and Chemical Toxicology*, **2019**, 130, 317-325.
 18. Angelova, V.T., **Pencheva, T.**, Vassilev, N., Simeonova, R., Momekov, G., Valcheva, V.. New indole and indazole derivatives as potential antimycobacterial agents, **2019**, *Medicinal Chemistry Research*, 28 (4), 485-49.
 19. Lagarde, N., Goldwaser, E. **Pencheva, T., Jereva, D., Pajeva, I.**, Rey, J., Tuffery, P., Villoutreix, B. O., Miteva, M. A., A Free Web-based Protocol to Assist Structure-based Virtual Screening Experiments, *International Journal of Molecular Sciences* (special issue *Recent Advances in Virtual Screening*), **2019**, 20(18), 4648.
 20. Dallavalle, S., Dobričić, V., Lazzarato, L., Gazzano, E., Machucheroe, M., **Pajeva, I., Tsakovska, I.**, Zidar, N., Fruttero, R., Improvement of conventional anti-cancer drugs as new tools against multidrug resistant tumors, *Drug Resistance Updates*, **2020**, 50, 100682.
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6. COORDINATOR

Full name of the coordinator organization

Institute of Biophysics and Biomedical Engineering
Bulgarian Academy of Sciences

Contact person

Prof. Tania Pencheva, PhD, Director of IBPhBME – BAS

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7. POSSIBLE PARTNERS

Indicate the partner
organizations

Full name of the partner

Inserm U1268, CNRS UMR CiTCoM – Univ. Paris Descartes, Faculté de Pharmacie
de Paris, 4 Av de l'Observatoire, 75270 Paris cedex 06, France

Contact person

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Full name of the partner

University of Siena

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Contact person

Mattia Mori, PhD, Senior Researcher

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8. IMPLEMENTED AND RUNNING PROJECTS

Projects related to
virology, vaccines,
infection diseases ...

1. *Multitarget peptide-fragment hybrids for the treatment of neurodegenerative diseases*, Bulgarian National Science Fund, Project KP-06-OPR03/8, 2018-2021, Project coordinator for the IBPhBME – BAS team: Assoc. Prof. Ivanka Tsakovska, PhD
2. *New diagnostic and therapeutic tools against multidrug resistant tumors*, EU Framework Programme Horizon 2020, COST Action CA17104, 2018-2022, Project leader for the IBPhBME – BAS team: Corr. Memb. Prof. Ilza Pajeva, D.Sc.

3. *New approach based on intercriteria data analysis for decision support in in silico research of complex biomolecular systems*, Bulgarian National Science Fund, Project DN 17/6, 2017-2020, Project leader: Prof. Tania Pencheva, PhD
4. *Mode of action networking and in silico co-targeting of host PPAR γ and host or viral proteins relevant to modulation of coronavirus-induced respiratory syndromes*, National program "Young scientists and Postdoctoral candidates" of Ministry of Education and Science, Postdoctoral Fellowship Module, 2020-2021, Postdoc: Senior Assist. Prof. Merilin Mazen Al Sharif, PhD, Supervisor: Corr. Member Prof. Ilza Pajeva, D.Sc.