SECOND INTERNATIONAL SYMPOSIUM ON BIOINFORMATICS AND BIOMEDICINE

OCTOBER 5–7, 2022
BURGAS, BULGARIA

info bio med

SECOND INTERNATIONAL SYMPOSIUM ON
BIOINFORMATICS AND BIOMEDICINE

OCTOBER 5–7, 2022
BURGAS, BULGARIA

info bio med

Organizers

"Prof. D-r Asen Zlatarov"
University – Burgas

Institute of Biophysics and Biomedical Engineering,
Bulgarian Academy of Sciences

INSTITUTE OF BIOPHYSICS AND BIOMEDICAL ENGINEERING

University Hospital
"Tsaritsa Yoanna-ISUL", Sofia

УМБАЛ ЦАРИЦА ЙОАННА-ИСУЛ

Union of Scientists in Bulgaria

UNION OF SCIENTISTS IN BULGARIA

Sponsors

Burgas Municipality

Top Hospital Service EAD

top hospital service

Fraport Twin Star Airport Management AD

Fraport Bulgaria

General Chairs

- Prof. Sotir Sotirov (BG)
- Prof. Tania Pencheva (BG)
- Acad. Chavdar Slavov (BG)
- Acad. Janusz Kacprzyk (PL)

Chairs of the Programme Committee

- Acad. Krassimir Atanassov (BG)
- Prof. Hristo Bozov (BG)

Programme Committee

- Corr. Member Prof. Ilza Pajeva (BG)
- Prof. Plamen Angelov (UK)
- Prof. Maia Angelova (AU)
- Prof. Oscar Castillo (MX)
- Prof. Panagiotis Chountas (UK)
- Prof. Plamen Ch. Ivanov (USA)
- Prof. Irena Jekova (BG)
- Prof. Vessela Krasteva (BG)
- Prof. Maciej Krawczak (PL)
- Prof. Said Melliani (MA)
- Prof. Patricia Melin (MX)
- Prof. Anthony Shannon (AU)
- Prof. Krasimira Tsaneva-Atanasova (UK)
- Prof. Ivanka Tsakovska (BG)
- Dr. Maria Miteva (FR)
- Dr. Jude D. Hemanth (IN)

Chairs of the Organizing Committee

- Prof. Evdokia Sotirova (BG)
- Prof. Galya Staneva (BG)

Organizing Committee

- Prof. Sashka Krumova (BG)
- Prof. Olympia Roeva (BG)
- Prof. Anelia Dobrikova (BG)
- Assoc. Prof. Vassia Atanassova (BG)
- Assoc. Prof. Veselina Bureva (BG)
- Assoc. Prof. Stanislav Simeonov (BG)
- Assoc. Prof. Peter Vassilev (BG)
- Assoc. Prof. Simeon Ribagin (BG)
- Stoyan Hristov (BG)

Contents

Invited Speakers

AI and Data-Driven Models for Precision Healthcare

Prof. Maia Angelova

School of IT at the Deakin University, Burwood Campus, Melbourne, Australia

Sleep and nutrition are essential and repeating processes which are vital for our quality of life and wellbeing. These processes involve complex dynamics and regulation at multi-scale that reflect developmental changes in mental and physical health, along with the day-to-day fluctuations. In this talk, I will share our current research in modelling insomnia and diabetes based on physical and physiological data, feedback mechanisms and interactions between networks at different scales.

Insomnia is a serious sleep disorder that remains under-diagnosed. We propose new machine learning models for classification of nocturnal awakenings in insomnia and healthy sleep from physical movements data. The models can distinguish acute from chronic insomnia and healthy sleep. They provide a robust basis for pre-screening of insomnia with wearable devices in a home environment. Glucose-insulin dynamics is central for understanding the regulation mechanisms between different organs in the human body and is key to maintain healthy life and prevent diabetes. We combine dynamical systems approach with machine learning algorithms to model the regulation between glucose and insulin and predict glucose dynamics and insulin utilisation in healthy and pre-diabetic regimes.

Curriculum Vitae

Maia Angelova is a Professor of Data Analytics and Machine Learning at Deakin University. Currently, she is the Director of the Data Analytics Research Lab at the School of IT. Maia joined Deakin in January 2017. Prior to this, she was a Professor of Mathematical Physics and Leader of the Mathematical Modelling Research Lab at Northumbria University at Newcastle upon Tyne since 2004 and before that a Lecturer in Physics in Somerville College at the University of Oxford from 1991 to 1996. Maia's research expertise and interests are in data-driven modelling of complex systems with specific interests in modelling sleep and insomnia, diabetes, dementia, depression, ageing and decision making. She has strong expertise in time series, spectral analysis, dynamical systems and symmetry. Maia's research is at the boundary between theory and applications. She is increasingly interested in translational research into the areas of health, medicine and healthcare. She has been funded by the Australian Defence, The Academy of Medical Sciences, EPSRC, MRC, European FP6 and FP7 Programs, The Royal Society, The London Mathematical Society, The Australian Mathematical Society and AMSI. She was the Coordinator and Principal Investigator of European Framework Program 7 Marie Curie Project MATSIQEL, "Models of ageing and technological solutions for improving and enhancing the quality of life" with 86 participants from 6 countries and 4 continents. Maia is a Fellow of The Institute of Physics, member of the Council of Complex Systems Society, member of Society of Mathematical Biology, The London Mathematical Society and The Australian Mathematical Society. She is an Associate Editor of the journals of Complexity, Frontiers of Physiology: Network Physiology, member of the Editorial Boards of Frontiers of Endocrinology, Frontiers of Physics, Bioinformatics and Biology Insights. She is a member of Program Committes and Technical Committees of several international conferences in mathematical physics, data science and complex systems.

Understanding Molecular Accumulation in Single Cells via Microfluidics and Mathematical Modelling

Prof. Krasimira Tsaneva-Atanasova

College of Engineering, Mathematics and Physical Sciences,
University of Exeter, United Kingdom

All living organisms exchange molecules with the environment. Organisms strive to take up molecules essential for subsistence such as sugars, amino acids and ions while simultaneously attempting to exclude poisonous molecules such as toxic waste and drugs. To achieve this aim, the cells constituting an organism are surrounded by membranes that act as physical barriers for unwanted molecules allowing for a controlled molecular exchange. These membranes are made up of lipids that are spanned by proteins that form several different physical pathways for molecular transport across the membrane. Understanding how these pathways help some cells to reduce the amount of toxic compounds they take up from the environment is a fundamental question in biology. In fact, there are important differences between cells even with the same genetic make-up. For example, in a population of Escherichia coli, commonly found in our intestine, some bacteria grow much slower than others. Even more surprisingly, some bacteria within the population are able to survive a quantity of antibiotic drugs that kills the rest of the population. In contrast, little is known about cell-to-cell differences in the ability to take up compounds and how the environment affects such capabilities. In this talk I will present our work so far on determining how can two genetically identical cells accumulate substantially different quantities of a given compound. To tackle this question we develop and use a novel combination of cross-disciplinary approaches drawing on complementary expertise in single cell microbiology, mathematics and omics.

Curriculum Vitae

Krasimira Tsaneva-Atanasova earned her undergraduate and MSc degrees in Mathematics at the University of Plovdiv, Bulgaria from 1991 until 1996. In September 2001 she started a PhD in Applied Mathematics at the University of Auckland, New Zealand. After completing her PhD in October 2004 she spent 18 months as a post-doctoral fellow at the Laboratory of Biological Modelling, National Institutes of Health, USA and another 15 months as a post-doctoral fellow at the Department of Mathematics and the Department of Biology at Ecole Normale Superieure in Paris, France. Krasimira joined the Department of Engineering Mathematics at the University of Bristol in October 2007 as a lecturer and was promoted to a Reader in Applied Mathematics in 2012. She moved to the College of Engineering, Mathematics and Physical Sciences, University of Exeter (UoE) in July 2013 where she is a Professor of Mathematics for Healthcare. Currently, Krasimira is the Associate Pro-Vice Chancellor for Research and Impact in the Faculty of Environment, Science and Economy at UoE (2022-2025).

Current Research Roles and Activities:

- EPSRC Strategic Advisory Network member (since 1st April 2021).
- Director of the EPSRC Hub for Quantitative Modelling in Healthcare (EP/T017856/1, 2021-2025).
- Living Systems Institute Assistant Director.
- Co-director of the University of Exeter ISSF TREE.
- Alan Turing Institute Fellow since October 2018.
- Hans Fischer Senior Fellow (since April 2019) at the Technical University of Munich (TUM) Institute for Advanced Study (IAS).
- Fellow of the Institute of Mathematics and its Applications (since April 2020).

Predicting Drug–Drug Interactions of Phase II Drug Metabolizing Enzymes

Dr. Maria A. Miteva

Centre National de la Recherche Scientifique, INSERM, France

Artificial Intelligence (AI) and Machine Learning (ML) are more than just buzz words being used in the pharmaceutical and biotechnology industry. There is now a steady stream of publications and evidence outlining what these terms really mean, how they can be applied in a drug discovery and development setting, and how much value they add in terms of saving time, effort and costs. AI and ML can be used for target identification, drug design and optimization, predicting drug toxicity and adverse events. We will present *in silico* study integrating structural bioinformatics and machine learning approaches to predict inhibition of drug-metabolizing enzyme. Drug metabolizing enzymes (DME) play a key role in the metabolism, elimination and detoxification of xenobiotics, drugs and endogenous molecules. While their principal role is to detoxify organisms by modifying compounds, such as pollutants or drugs in some cases they render their substrates more toxic thereby inducing adverse drug reactions, or their inhibition can lead to drug-drug interactions. Predicting potential inhibition of DME is important in early-stage drug discovery. We focus on Cytochrome P450 (CYP) responsible for the metabolism of 90 % drugs and on sulfotransferases (SULT), phase II conjugate drug metabolizing enzymes, acting on a large number of drugs, hormones and natural compounds. We performed modeling using two learning algorithms, Support Vector Machine (SVM) and RandomForest combining chemicals, protein-ligand interactions and protein structure and dynamics information. Our inhibition models predict CYP and SULT inhibition for three isoforms with an accuracy of >80 % and are implemented in the new software DrugME.

Curriculum Vitae

Maria Miteva is a Research Director at INSERM. She has been working in Bulgaria (Bulgarian Academy of Sciences), Sweden (Karolinska Institutet), and France (CNRS, Inserm). She joined INSERM in 2002 and is currently co-directing the INSERM Unit ERL U1268 “Medicinal Chemistry and Translational Research”, at the Faculty of Pharmacy, University of Paris. She has strong expertise in medicinal chemistry, biophysics, drug-drug interactions, bioinformatics, chemoinformatics and AI for drug discovery and toxicity prediction. She has 4 patents and more than 100 peer-reviewed publications (ID ORCID: N-2419-2018). She edited the book “*In silico* lead discovery“ (Bentham Sci 2011). She is an editorial board member for several reputed journals in the field and an Associated Editor for BMC Pharmacology and Toxicology.

Current Challenges and Current Solutions in Biomedical Data Science: Personalisation; Explainability; Multi-modality; Model Adaptation

Prof. Nikola Kasabov

Auckland University of Technology, Auckland, New Zealand

The talk presents 4 current challenges in biomedical data science, namely:

1. Personalised modelling for early diagnosis and prognosis of a disease.
2. Explainability and profiling at a personal level for a better treatment.
3. Multiple modality of data, such as genetic, clinical, behaviour, cognitive, static, temporal.
4. Incremental adaptability of the models with new data being made available continuously.

The talk presents also current solutions, such as Evolving Connectionist Systems (ECOS) and brain-inspired spiking neural networks (SNN) developed by the author and his team. The ECOS models, such as EFuNN and DENFIS [1, 2] offer efficient solutions to all challenges from 1 to 4 above on vector-based data, while SNN, such as NeuCube [2, 3] offer a general solution for integrated vector-based and temporal data, including longitudinal data. The talk describes briefly the two classes of models (ECOS and SNN NeuCube) and how they can be used to address the above 4 challenges.

Experimental results from several projects led by the author are discussed, including:

- Early diagnosis and personalised profiling of cancer.
- Predicting AD from longitudinal MRI and multimodal data.
- Personalised prediction of stroke.
- Predicting response to treatment of drug addicts and patients of Schizophrenia.
- Early diagnosis of Psychosis and Schizophrenia based on genetic and cognitive data.

The above applications have been developed in the development software NeuCom [2] and NeuCube [4], which are available free.

References

[1] N. Kasabov, Evolving Connectionist Systems, Springer, 2007.
[2] NeuCom, https://theneucom.com.
[3] N. Kasabov, Time-Space, Spiking Neural Networks and Brain-Inspired Artificial Intelligence, Springer, 2019, https://www.springer.com/gp/book/9783662577134.
[4] NeuCube, https://kedri.aut.ac.nz/neucube.

Curriculum Vitae

Professor Nikola (Nik) K. Kasabov (also known as Kassabov) is Life Fellow of IEEE, Fellow of the Royal Society of New Zealand, Fellow of the INNS College of Fellows, DVF of the Royal Academy of Engineering UK. He is the Founding Director of the Knowledge Engineering and Discovery Research Institute (KEDRI), Auckland and Professor at the School of Engineering, Computing and Mathematical Sciences at Auckland University of Technology, New Zealand. He is also George Moore Chair Professor of Data Analytics at the University of Ulster UK, Honorary Professor at the Teesside University UK and the University of Auckland NZ, Visiting Professor at the IICT Bulgarian Academy of Sciences and Peking University in Shenzhen. Kasabov is Past President of the Asia Pacific Neural Network Society (APNNS) and the International Neural Network Society (INNS). He has been a chair and a member of several technical committees of IEEE Computational Intelligence Society and Distinguished Lecturer of IEEE (2012-2014). He is Editor of Springer Handbook of Bio-Neuroinformatics, EIC of Springer Series of Bio-and Neuro-systems and co-EIC of the Springer journal Evolving Systems. He is Associate Editor of several journals, including Neural Networks, IEEE TrNN, Tr CDS, Information Sciences, Applied Soft Computing. Kasabov holds MSc and PhD from TU Sofia, Bulgaria. His main research interests are in the areas of neural networks, intelligent information systems, soft computing, bioinformatics, neuroinformatics. He has published more than 700 publications, highly cited internationally. He has extensive academic experience at various academic and research organisations in Europe and Asia, including: TU Sofia Bulgaria; University of Essex UK; University of Otago, NZ; Shanghai Jiao Tong University and CASIA China, ETH/University of Zurich. He is currently a Visiting Professor at the IICT Bulgarian Academy of Sciences, Peking University in Shenzhen and Dalian University China. Kasabov has received a number of awards, among them: Doctor Honoris Causa from Obuda University; INNS Ada Lovelace Meritorious Service Award; NN journal Best Paper Award for 2016; APNNA 'Outstanding Achievements Award'; INNS Gabor Award for 'Outstanding contributions to engineering applications of neural networks'; EU Marie Curie Fellowship; Bayer Science Innovation Award; APNNA Excellent Service Award; RSNZ Science and Technology Medal; 2015 AUT NZ Medal; Medal "Bacho Kiro" of the SU Pavlikeni, Honorary Member of the Bulgarian, the Greek and the Scottish Societies for Computer Science, Honorary Citizen of Pavlikeni – Bulgaria. More information of Prof. Kasabov can be found from: https://academics.aut.ac.nz/nkasabov. Born Svistov Bulgaria. Daughters: Kapka Kassabova, Assia Kassabova. Wife: Diana Kassabova.

Efficiently Handling Textual Data in Medical Applications: A Novel Approach

Prof. Guy De Tré

Ghent University, Ghent, Belgium

A considerable part of medical information is available as textual data. This textual data can have different manifestations including medical reports, prescriptions, emails, scientific publications, spreadsheet data, patient enquiries, and so on. Medical decision making and data analysis could benefit enormously if the right data, independent of its format, would be available for the decision maker at the right time. Conventional information management mainly focusses on structured data that are stored in relational databases. Efficiently integrating and including textual data in such systems is challenging because of the lack of a fixed common structure and the complexity of written language. In this presentation we will introduce a novel approach to handle and include medical textual data in decision making. This approach avoids information loss, efficiently copes with context and provides a common meta-level structure, which is based on Who-What-When-Where (4W) component identification. This proposed model supports SQL-based querying, exploration, integration, analysis and summarization of large heterogeneous medical data collections. Furthermore, open challenges related to the handling of data imperfections and data veracity are illustrated and perspectives for further research are proposed.

Curriculum Vitae

Guy De Tré is a Full Professor at the Department of Telecommunications and Information Processing of the Faculty of Engineering and Architecture of Ghent University where he is heading the research group on Database, Document, and Content Management (DDCM). His research activities are centred on computational intelligence in information management systems, including fundamental research on uncertainty handling, multi-valued logics and spatio-temporal modelling and applied research on, among others, big data (NoSQL databases), information fusion, flexible querying, decision support, data quality, and unstructured data. He is (co)author of more than 280 scientific publications. He is area editor of the 'International Journal of Computational Intelligence Systems', Board member of the European Society for Fuzzy Logic and Technology (EUSFLAT) and steering committee member of Flexible Querying Answering (FQAS).

Type-2 and Type-3 Fuzzy Systems: Theory and Applications

Prof. Oscar Castillo

Tijuana Institute of Technology, Tijuana, Mexico

Type-2 fuzzy systems are powerful intelligent models based on the theory of fuzzy sets, originally proposed by Prof. Zadeh. Most real-world applications up to now are based on type-1 fuzzy systems, which are built based on the original (type-1) fuzzy sets that extend the concept of classical sets. Type-2 fuzzy sets extend type-1 fuzzy sets by allowing the membership to be fuzzy, in this way allowing a higher level of uncertainty management. Even with the current successful applications of type-1 fuzzy systems, now several papers have shown that type-2 is able to outperform type-1 in control, pattern recognition, manufacturing and other areas. The key challenge in dealing with type-2 fuzzy models is that their design has a higher level of complexity, and in this regard the use of bio-inspired optimization techniques is of great help in finding the optimal structure and parameters of the type-2 fuzzy systems for particular applications, like in control, robotics, manufacturing and others. Methodologies for designing type-2 fuzzy systems using bio-inspired optimization in different areas of application are presented as illustration. Finally, the prospects for the future trends and applications of type-3 fuzzy logic will be discussed.

Curriculum Vitae

Prof. Oscar Castillo holds the Doctor in Science degree (Doctor Habilitatus) in Computer Science from the Polish Academy of Sciences (with the Dissertation “Soft Computing and Fractal Theory for Intelligent Manufacturing”). He is a Professor of Computer Science in the Graduate Division, Tijuana Institute of Technology, Tijuana, Mexico. In addition, he is serving as Research Director of Computer Science and head of the research group on Hybrid Fuzzy Intelligent Systems. Currently, he is the President of HAFSA (Hispanic American Fuzzy Systems Association) and Past President of IFSA (International Fuzzy Systems Association). Prof. Castillo is also Chair of the Mexican Chapter of the Computational Intelligence Society (IEEE). He also belongs to the Technical Committee on Fuzzy Systems of IEEE and to the Task Force on “Extensions to Type-1 Fuzzy Systems”.

He is also a member of NAFIPS, IFSA and IEEE. He belongs to the Mexican Research System (SNI Level 3). His research interests are in Type-2 Fuzzy Logic, Fuzzy Control, Neuro-Fuzzy and Genetic-Fuzzy hybrid approaches. He has published over 300 journal papers, 10 authored books, 40 edited books, 200 papers in conference proceedings, and more than 300 chapters in edited books, in total 886 publications according to Scopus (H-index = 62), and more than 1000 publications according to ResearchGate (H-index = 73 in Google Scholar). He has been Guest Editor of several successful Special Issues in the past, like in the following journals: Applied Soft Computing, Intelligent Systems, Information Sciences, Non-Linear Studies, Fuzzy Sets and Systems, JAMRIS and Engineering Letters.

He is currently an Associate Editor of the Information Sciences Journal, Applied Soft Computing Journal, Engineering Applications of Artificial Intelligence, Granular Computing Journal and the International Journal on Fuzzy Systems. Finally, he has been elected IFSA Fellow in 2015 and MICAI Fellow member in 2017. He has been recognized as Highly Cited Researcher in 2017 and 2018 by Clarivate Analytics for his multiple highly cited papers in Web of Science.

Session

Data Mining in Biomedicine and Healthcare

Parallel Technique on Bidirectional Associative Memory Cohen–Grossberg Neural Network

Gani Stamov [1], **Stanislav Simeonov** [2], **Ivan Torlakov** [2], **Marina Yaneva** [3]

[1] *Technical University of Sofia*
Sliven 8800, Bulgaria
gstamov@abv.bg
[2] *Department of Computer Systems and Technologies*
"Prof. Dr. Assen Zlatarov" University
1 "Prof. Yakimov" Blvd., Burgas 8010, Bulgaria
stanislav_simeonov@btu.bg, itorlakov@gmail.com
[3] *Department of Social Health and Healthcare "*
Prof. Dr. Assen Zlatarov" University
1 "Prof. Yakimov" Blvd., Burgas 8010, Bulgaria
marinaiaaneva@abv.bg

Abstract: The present paper is devoted to software analysis on applied method used on parallel technology, in particular CUDA and OpenMPI, to find stable areas of single mathematical model of Bidirectional Associative Memory (BAM) Cohen–Grossberg neural network with time-varying delays. The given type of neural networks gives opportunity of modelling and study of biological problems.

Keywords: Neural network, Cohen–Grossberg, Parallelism, CUDA, Open-MPI.

Acknowledgements: This research was funded in part by the European Regional Development Fund and the Operational Program "Science and Education for Smart Growth" under Contract UNITe No. BG05M2OP001-1.001-0004-C01 (2018-2023).

Prediction of the Granulometric Composition of the Silt Loading on Transport Arteries in the City of Bourgas Based on Artificial Neural Networks

Dimitrinka Ivanova [0000-0002-8949-3715], **Yordanka Tasheva** [0000-0003-3638-6622], **Evdokia Sotirova** [0000-0001-6178-5356], **Aleksandar Dimitrov** [0000-0002-2683-2222], **Sotir Sotirov** [0000- 0003-1292-6225]

"Prof. Dr. Assen Zlatarov" University
1 "Prof. Yakimov" Blvd., Burgas 8010, Bulgaria
divanova@btu.bg, jtasheva_2006@abv.bg,
esotirova@btu.bg, adimitrov@uniburgas.bg,
ssotirov@btu.bg

Abstract: This study integrates data from laboratory road silt analyses and predicts these values using artificial neural networks. It is known that the emissions from vehicular traffic are a significant contributor to total particulate matter (PM) concentrations in urban areas and have detrimental effects on human health. The characteristics of these emissions, from different traffic-related sources, are essential to study their impact on human health. The deposition of particulate matter (road silt) on road surfaces and its suspension from roadways is the main mechanism by which road transport causes secondary PM pollution. The analysis of road silt was performed by sieve and laser diffraction analyses. The obtained data were used to predict the grain size composition of the fractions below 75 μm from the road silt samples, by neural networks, after sampling along the main and secondary traffic arteries of the city of Burgas, and analyzing the fractions up to 75 μm.

Keywords: Neural network, Silt loading, Granulometric composition, Transport arteries.

Acknowledgements: This research has been supported by Contract No. КП-06-Н27/12 of 11.12.2018 "Modeling and elaboration of complex system for selection of transport technology in transport network" funded by the National Science Fund of the Ministry of Education and Science of Bulgaria.

An Intuitionistic Fuzzy Estimation Approach to Magnetic Resonance Imaging

Sotir Sotirov, Todor Kostadinov, Stoyan Hristov

"Prof. Dr. Assen Zlatarov" University
1 "Prof. Yakimov" Blvd., Burgas 8010, Bulgaria
ssotirov@btu.bg, kostadinov.todor@yahoo.com,
hristov@dr.com

Abstract: This work addresses a novel approach of image estimation using fuzzy logic. The research aims to devise a technique for estimating the quality of tomographic images by measuring the level of uncertainty on an image of interest. This approach can be applied in order to improve the quality of a tomographic image of human bones and thus improve the resulting image, especially in case of fracture or anomaly without compromising it. In order to verify the approach, an experiment on real tomographic images has been carried out.

Keywords: Tomography, Tomographic image estimation, Fuzzy logic.

Acknowledgements: The authors are thankful for the support provided by the European Regional Development Fund and the Operational Program "Science and Education for Smart Growth" under Contract UNITe No. BG05M2OP001-1.001-0004-C01 (2018-2023).

Water Safety and Toxicity Assessment Using Real Time Sensor Measurements and Fuzzy Logic Data Processing

Hyusein Yemendzhiev [1], **Plamena Zlateva** [2], **Valentin Nenov** [1]

[1] *"Prof. Dr. Assen Zlatarov" University*
1 "Prof. Yakimov" Blvd., Burgas 8010, Bulgaria
hyemendzhiev@btu.bg, vnenov@btu.bg
[2] *Institute of Robotics, Bulgarian Academy of Sciences*
Acad. Georgi Bonchev Str., Bl. 2, Sofia 1113, Bulgaria
plamzlateva@abv.bg

Abstract: The water quality monitoring is a crucial part of the efficient water management. However, the conventional chemical analyses could not offer real time toxicity assessment which creates significant risks for human and ecosystems health. Analysing the entire diversity toxic compounds, potentially presented in the water is not an easy, nor economical task and sometimes it is impossible, as well. This group of chemicals varies from heavy metals ions to complex organic molecules and bio-toxins. Finding a general indicator for the toxicity presented in water and aquatic environments could be an important step toward the development of early warning systems to support decision making in water monitoring.

In this study, Fuzzy logic approach is used for integration and evaluation of the specific signal patterns obtained from pH and electro conductivity measurement combined with the data received from a custom build bio-electrochemical sensor. Two different scenarios were studied, being model cases of organic toxic compounds and heavy metals in fresh water.

Keywords: Toxicity evaluation, Hazardous materials, Water, Fuzzy logic.

Acknowledgements: The authors are thankful for the support provided by the European Regional Development Fund and the Operational Program "Science and Education for Smart Growth" under Contract UNITe No. BG05M2OP001-1.001-0004-C01(2018-2023).

Generalized Net Model of Multimodal Biometric System for Authenticating an Individual by Keystroke Dynamics and Eye Tracking Techniques

Veselina Bureva, Todor Petkov, Stanislav Popov

Laboratory of Intelligent Systems
"Prof. Dr. Assen Zlatarov" University
1 "Prof. Yakimov" Blvd., Burgas 8010, Bulgaria
vbureva@btu.bg, todor_petkov@btu.bg,
stani_popov@yahoo.com

Abstract: In the current research work the behavioral biometrics eye tracking and keystroke dynamics are investigated. The methods are frequently used for integration between patients and medical devices. A GN model of the multimodal biometric system is constructed. It monitors the process of behavioral biometrics eye tracking and keystroke dynamics. The optimization step is added to provide the necessity for better results.

Keywords: Biometrics, Behavioral biometrics, Generalized nets, Multimodal biometric system.

Acknowledgements: The authors are thankful for the support provided by Project "Analysis and modelling of artificial intelligence algorithms and their application", No. NIH – 462/2021.

Emotion Recognition Using a Convolutional Neural Network

Todor Petkov, Aleks Titanyan, Veselina Bureva, Stanislav Popov

"Prof. Dr. Assen Zlatarov" University
1 "Prof. Yakimov" Blvd., Burgas 8010, Bulgaria
todor_petkov@btu.bg, titanyan.aleks@gmail.com,
vbureva@btu.bg, stani_popov@yahoo.com

Abstract: Human emotions are significant to a person's mental health. In the field of Affective Computing human emotions are one of the main subjects that play an important role. In order to observe emotions of the human a lot of characteristics can be used such as speech, skin responses, heart rate or facial expressions. In the paper the process of emotion recognition using artificial neural network is described. The training set consists of grayscale images which are 48×48 pixels and are divided into 7 categories Angry, Disgust, Fear, Happy, Sad, Surprise, Neutral. The Convolutional Neural Network is used for the purpose of emotion recognition along with its pooling and convolutional layers. At the end of the process the trained neural network can successfully recognize the human emotion.

Keywords: Emotion Recognition, Artificial Neural Network, Convolutional Neural Network.

Acknowledgements: The authors are thankful for the support provided by Project "Analysis and modelling of artificial intelligence algorithms and their application", No. NIH – 462/2021.

3D Technologies in Urological Practice. Application of Software for 3D Processing in Urological Practice

Zlatka Cholakova, Nikolay Mirinchev

Department of Urology
University Hospital for Active Treatment
73 Stefan Stambolov Str., Burgas 8000, Bulgaria
z_cholakova@yahoo.com, drmirinchev@abv.bg

Abstract: The aim of our research is to use free software for 3D processing of ICOM files to predict the duration of laser lithotripsy in a group of stones with different 3D configurations and to show the application of 3D reconstructions in real urological practice. To show the advantages of preoperative counseling with the help of this software and to reflect this in the individual approach in each case when planning the operative intervention – the stages and selection of the most appropriate operative approach for the patient, choice of tools and energy source.

Keywords: 3D reconstruction, Preoperative evaluation, Software, Urolithiasis.

Session

Decision Making in Biomedicine and Healthcare

InterCriteria Analysis of Data Obtained from Patients with Hypercholesterolemia Treated with Linoprixol

Valentin Vassilev [1,2], **Hristo Hlebarov** [1], **Simeon Ribagin** [3,4], **Krassimir Atanassov** [3,5]

[1] *University Hospital Burgas, Burgas, Bulgaria*
vailvasilev@mail.bg, hhlebarov@gmail.com
[2] *Faculty of Public Health and Health Care,*
"Prof. Dr. Assen Zlatarov" University
1 "Prof. Yakimov" Blvd., Burgas 8010, Bulgaria
[3] *Department of Bioinformatics and Mathematical Modelling*
Institute of Biophysics and Biomedical Engineering
Bulgarian Academy of Sciences
Acad. Georgi Bonchev Str., Bl. 105, Sofia 1113, Bulgaria
simribagin@gmail.com, k.t.atanassov@gmail.com
[4] *Department of Health and Pharmaceutical care, Medical College*
"Prof. Dr. Assen Zlatarov" University
1 "Prof. Yakimov" Blvd., Burgas 8010, Bulgaria
[5] *Intelligent Systems Laboratory,*
"Prof. Dr. Assen Zlatarov" University
1 "Prof. Yakimov" Blvd., Burgas 8010, Bulgaria

Abstract: The purpose of the present paper is to present the effects of the alternative treatment of patients with hypercholesterolemia with Linoprixol. The method of InterCriteria Analysis was applied to study the dependencies between the total cholesterol, LDL and triglycerides levels obtained in a clinical trial period conducted in the Vascular Surgery Clinic of University Hospital Burgas.

Keywords: InterCriteria analysis, Hypercholesterolemia, Linoprixol.

Acknowledgements: The present research is supported under Grant No. KP-06-N-22/1 "Theoretical research and applications of InterCriteria Analysis" of the National Science Fund of Bulgaria.

ABO System Blood Groups Distribution in Bulgaria, Based on a Dataset of the Patients of the University Hospital "Saint Anna", Sofia, Bulgaria, from 2015 to 2021

Vassia Atanassova [1, [0000-0002-3626-9461]], **Nikolay Andreev** [2], **Angel Dimitriev** [1]

[1] *Institute of Biophysics and Biomedical Engineering*
Bulgarian Academy of Sciences
Acad. Georgi Bonchev Str., Bl. 105, Sofia 1113, Bulgaria
vassia.atanassova@gmail.com, angel_dimitriev@abv.bg

[2] *Transfusion Hematology Department*
University Hospital "Saint Anna"
1 D. Mollov Str., Mladost 1, Sofia 1750, Bulgaria
imuno_chem@abv.bg

Abstract: The paper presents the analysis of a dataset containing the records of 47562 Bulgarian individuals, patients of the University Hospital "Saint Anna", Sofia, Bulgaria in the period from 1 January 2015 to 31 December 2021, and aims at the establishing the distribution of blood groups of the ABO system and the frequencies of the A1 and A2 subgroups and the Rh(D) antigen. In the frames of the conducted research, a series of data cleansing and data extraction procedures have been applied. The statistical analysis established the following frequencies of the ABO system blood groups in this sample of the Bulgarian population: A – 43.66%, B – 16.36%, O – 31.87% and AB – 8.11%. The prevalence of Rh(D) antigen determined was 86.38%. The distributions of A1 and A2 subgroups in the A group were determined as 91.92% and 8.09%, respectively, and the distributions of A1B and A2B subgroups in the AB group were established as 88.52% and 11.48%. These results are compared to the findings of other researchers regarding the distribution of ABO blood system blood antigens among the Bulgarian population, and slightly updates the results from the dataset of the patients of that Hospital from the period 2015–2020.

Keywords: ABO system, Blood group distribution, Rh(D) antigen distribution, ABO blood groups distribution in Bulgaria.

Acknowledgements: The authors are grateful for the support provided under Grant No. KP-06-N-22/1 "Theoretical research and applications of InterCriteria Analysis" of the National Science Fund of Bulgaria.

InterCriteria Analysis of the Geographic Distribution of the ABO System Blood Groups in the Patients of the University Hospital "Saint Anna", Sofia, Bulgaria, from 2015 to 2021

Vassia Atanassova [1, [0000-0002-3626-9461]], **Nikolay Andreev** [2], **Angel Dimitriev** [1]

[1] *Institute of Biophysics and Biomedical Engineering*
Bulgarian Academy of Sciences
Acad. Georgi Bonchev Str., Bl. 105, Sofia 1113, Bulgaria
vassia.atanassova@gmail.com, angel_dimitriev@abv.bg

[2] *Transfusion Hematology Department*
University Hospital "Saint Anna"
1 D. Mollov Str., Mladost 1, Sofia 1750, Bulgaria
imuno_chem@abv.bg

Abstract: The paper presents the results of the application of the method of InterCriteria Analysis on a dataset of the blood group of 47562 Bulgarian individuals, patients of the University Hospital "Saint Anna", Sofia, Bulgaria collected in the period from 2015 to 2021. Apart of the ABO system blood groups, the recorded data contain information about the patients' A1 and A2 subgroups and the Rh(D) antigen. In the current leg of research, in addition to the easily extracted information about the patients' year of birth and sex, here for the first time, the patients' birthplace regions are algorithmically extracted on the basis of the recorded personal identification numbers. This allows us to have a deeper and more insightful picture of the regional distribution of the frequencies of the ABO system, A1 and A2 subgroups and the Rh(D) antigen in the frames of the Bulgarian population, which is a level of detail that has not been yet reported in the existing literature and is considered an important contribution of the current research work to the state-of-the-art. The conducted InterCriteria Analysis on these data gives additional details that may help decision makers on national and regional level with respect to regional and cross-regional demand and supply of blood and blood products in Bulgaria.

Keywords: ABO system, Blood group distribution, Rh(D) antigen distribution, ABO blood groups distribution in Bulgaria, InterCriteria analysis, Intuitionistic fuzzy sets.

Acknowledgements: The authors are grateful for the support provided under Grant No. KP-06-N-22/1 "Theoretical research and applications of InterCriteria Analysis" of the National Science Fund of Bulgaria.

Rhythm Analysis during Cardio-pulmonary Resuscitation with Convolutional and Recurrent Neural Networks Using ECG and Optional Impedance Input

Vessela Krasteva [0000-0001-5385-2109], **Irena Jekova** [0000-0002-8626-7819]

Institute of Biophysics and Biomedical Engineering, Bulgarian Academy of Sciences
Acad. Georgi Bonchev Str., Bl. 105, Sofia 1113, Bulgaria
{vessika,irena}@biomed.bas.bg

Abstract: Chest compressions (CC) during cardiopulmonary resuscitation (CPR) produce strong artifacts in the electrocardiogram (ECG) via defi-pads. Heart rhythm can hardly be determined visually, but also by the shock-advisory algorithms in automated external defibrillators (AED). This study aims to investigate the potential of deep neural networks (DNN) as a powerful unsupervised feature extraction and classification algorithm that can give a shock advisory decision during CPR, regardless of the CC fraction in the analysis interval. Our research objective is focused on detecting whether the rhythm is shockable or non-shockable from the primary raw ECG input, but also to verify the hypothesis that the secondary impedance (IMP) channel, which is generally modulated by the thorax movements and correlated to CC artifacts may contribute to performance. We designed 7 DNN architectures for processing of one (ECG) or two (ECG, IMP) input channels, involving fully-convolutional or convolutional-recurrent layers (LSTM or BiLSTM). In 30:2 compression-to-ventilation CPR during out-of-hospital cardiac arrest, the start of the CC period preceding the regular AED rhythm analysis was used as a time anchor to extract 62987 CPR strips (ECG, IMP) at 5 offsets (–10 s, –5 s, 0 s, +5 s, +10 s), thus representative of different CC durations in the analysis interval (10 s). They are divided patient-wise to training/test datasets: 1797/1747 ventricular fibrillations (VF), 730/768 normal sinus rhythms (NSR), 8583/8226 other non-shockable rhythms (ONR), 21609/19527 asystoles. Comparative study rejects the hypothesis that the impedance contributes to efficiency of the rhythm analysis during CPR, considering that DNNs with two (ECG, IMP) inputs have specificity drop up to 3% points for non-shockable rhythms compared to one (ECG) input. The use of a recurrent layer after fully-convolutional architecture adds about 1% improvement in VF sensitivity (93.8%), keeping compatible specificity for Asystole (95.6%), NSR (99.2%), ONR (96.8%). The applied deep learning strategy justifies that convolutional-recurrent DNN architectures with a single ECG input are able to satisfy AHA recommendations for rhythm analysis with an arbitrary CC fraction distribution during CPR.

Keywords: Deep learning, ECG, Impedance, AED, Ventricular fibrillation, Chest compressions, CPR, CNN, LSTM, BiLSTM.

Acknowledgements: This work was supported by the Bulgarian National Science Fund, Grant No. КП-06-Н42/3 “Computer aided diagnosis of cardiac arrhythmias based on machine learning and deep neural networks”.

Convolutional Autoencoder for Filtering of Power-line Interference with Variable Amplitude and Frequency: Study of 12-lead PTB-XL ECG Database

Kamen Ivanov, Irena Jekova [0000-0002-8626-7819], **Vessela Krasteva** [0000-0001-5385-2109]

Institute of Biophysics and Biomedical Engineering
Bulgarian Academy of Sciences
Acad. Georgi Bonchev Str., Bl. 105, Sofia 1113, Bulgaria
{kamen,vessika,irena}@biomed.bas.bg

Abstract: This study aims to explore a new deep learning strategy for electrocardiogram (ECG) denoising under adverse conditions of non-stationary power-line interference (PLI) with amplitude changes or nominal frequency deviations. The study presents an exhaustive training strategy of deep convolutional autoencoder (CAE), while input with one of the largest PhysioNet 12-lead ECG databases contaminated by simulated sinusoidal PLI noise with augmented settings. Twelve ECG leads (I, II, III, aVR, aVL, aVF, V1–V6) from 14890 PTB-XL records, divided patient-wise to training (50%, 7441 records), validation (20%, 2979 records) and test (30%, 4470 records) are superimposed by PLI with five signal-to-noise ratios (SNR) (–2.5, 0, 2.5, 5, 7.5 dB), nine frequencies (48, 48.5, 49, 49.5, 50, 50.5, 51, 51.5, 52 Hz), 12 amplitude slew rates ±(50, 100, 250, 500, 750, 1000 μV/s), and 14 frequency slew rates ±(0.01, 0.025, 0.05, 0.075, 0.1, 0.15, 0.2 Hz/s). CAE receptive field inputs one ECG lead with 1024 samples (2.048 s for 500 Hz sampling rate). CAE architecture is designed with seven 1D-convolutional layers, including three encoder layers (filters × kernel size = 16×8, 8×8, 8×8) and four decoder layers (8×8, 8×8, 16×8, 1×8) with linear activation function and same padding. CAE non-linear operations for max-pooling and up-sampling (pool size of 2) follow each encoder and decoder convolutional layers, respectively. Adam optimizer and mean squared error loss function are applied for CAE training over 250 epochs. The quality of clean ECG reconstruction in CAE output is evaluated by root-mean-square error (RMSE), percentage-root-mean-square difference (PRD) and improvement in signal-to-noise ratio (SNR_{imp}). Statistical test results for denoising of all 12 ECG leads present median RMSE = 5.3 μV, PRD = 3.5%, SNR_{imp} = 22–32 dB for SNR = –2.5 to 7.5 dB. The results do not substantially change for PLI frequencies 48–52 Hz, amplitude slew rates up to ±1000 μV/s and frequency slew rates up to ±0.2 Hz/s with median value divergence of ΔRMSE < 2 μV, ΔPRD < 1.5%, $\Delta SNR_{imp} \leq 3$ dB. The observed performance stability justifies the deep learning strategy for training a CAE with generalizable application for denoising of unseen ECG signals with non-stationary PLI.

Keywords: Electrocardiogram, Deep learning, Artificial neural networks, Denoising autoencoder, Digital filters, Signal-to-noise ratio, 50 Hz filtering.

Acknowledgements: This work was supported by the Bulgarian National Science Fund, Grant No. КП-06-Н42/3 “Computer aided diagnosis of cardiac arrhythmias based on machine learning and deep neural networks”.

Multicriteria Analysis of Oncology Data during the Covid-19 Pandemic

Evdokia Sotirova [1], **Hristo Bozov** [1,2], **Sotir Sotirov** [1], **Greta Bozova** [3], **Simeon Ribagin** [4], **Vladimir Gonchev** [1]

[1] *"Prof. Dr. Assen Zlatarov" University*
1 "Prof. Yakimov" Blvd., Burgas 8010, Bulgaria
hr_bozov@yahoo.com, esotirova@btu.bg, ssotirov@btu.bg, gonchev@gmail.com
[2] *Oncology Complex Center – Burgas,*
86 Demokratsiya Blvd., Burgas 8000, Bulgaria
[3] *Department of Nephrology, Military Medical Academy*
3 George Sofiiski Str., Sofia 1606, Bulgaria
greti@abv.bg
[4] *Institute of Biophysics and Biomedical Engineering*
Bulgarian Academy of Sciences
Acad. Georgi Bonchev Str., Bl. 105, Sofia 1113, Bulgaria
simribagin@gmail.com

Abstract: In the paper, data related to the treatment of Covid-19 patients for the period 28.10.2020-23.3.2022 were investigated. Some of the patients are with oncological diseases. The studied patients were admitted to a hospital in the city of Burgas, specialized in the treatment of cancer. The data contains information about the name of the disease according to the International Statistical Classification of Diseases and Health Problems (ICD), period of the patient's hospitalization, number of patients, medical staff by profile, etc. The method of InterCriteria Analysis was applied to study the dependencies between the parameters describing the patients and the medical staff. A self-organized neural network was developed for clustering the information related to the type of cancer.

Keywords: InterCriteria Analysis, Covid-19, Oncological disease, Self-organized neural network, Intuitionistic Fuzzy Logic.

Acknowledgements: This research is supported under Grant No. KP-06-N-22/1 "Theoretical research and applications of InterCriteria Analysis" of the National Science Fund of Bulgaria.

Emotional Intelligence of Students during Pandemic Outbreak. A Study in Higher Education

Milen Todorov [1], **Gergana Avramova-Todorova** [1], **Veselina Bureva** [1], **Maciej Krawczak** [2], **Cengiz Kahraman** [3]

[1] *"Prof. Dr. Assen Zlatarov" University*
1 "Prof. Yakimov" Blvd., Burgas 8010, Bulgaria
mtodorov@btu.bg, g.avramova@abv.bg, vesito_ka@abv.bg, ssotirov@btu.bg
[2] *Warsaw School of Information Technology*
Systems Research Institute, Polish Academy of Sciences
6 Newelska Str., Warsaw 01-447, Poland
krawczak@ibspan.waw.pl
[3] *Istanbul Technical University, Management Faculty*
Macka, Besiktas, 34367, Istanbul, Turkey
kahramanc@itu.edu.tr

Abstract: Emotional intelligence is a main area in educational psychology and a key factor in the academic life of students. In the current study the dimensions of emotional intelligence – self-awareness, managing emotions, motivating oneself, and social skills were examined in order to identify negatively affected aspects due to the COVID 19 outbreak. Data was gathered from students from University "Prof. Dr. Assen Zlatarov", Burgas, Bulgaria through a self-completion electronic questionnaire which includes a total of 50 questions related to emotional intelligence. The obtained results are processed by making use of intuitionistic fuzzy set (IFS) techniques. It was found that there is no significant influence of the pandemic situation on the emotional condition of the students. However, a set of elements associated with the dimensions of emotional intelligence should be taken into account in order to support the success of students during their education and further professional realization.

Keywords: Emotional intelligence, COVID 19 outbreak, Academic learning.

Acknowledgements: The authors are thankful for the support provided by the European Regional Development Fund and the Operational Program "Science and Education for Smart Growth" under Contract UNITe No. BG05M2OP001-1.001-0004-C01(2018-2023).

Session

Bioinformatics and Computational Biology

Bioinformatics and Biostatistical Models for Analysis and Prognosis of Antimicrobial Resistance

Maya Zhelyazkova [1], **Roumyana Yordanova** [2], **Iliyan Mihaylov** [1], **Stefan Tsonev** [3], **Dimitar Vassilev** [1]

[1] *Faculty of Mathematics and Informatics*
Sofia University "St. Kliment Ohridski"
5 James Bourchier Blvd., Sofia 1164, Bulgaria
zhelyazkova@fmi.uni-sofia.bg,
iliqn.mihailov.92@gmail.com,
dimitar.vassilev@fmi.uni-sofia.bg
[2] *Bulgarian Academy of Sciences,*
Institute of Mathematics and Informatics
Acad. Georgi Bonchev Str., Bl. 8, Sofia 1113, Bulgaria
roumyana.yordanova@gmail.com
[3] *AgroBioInstitute,*
8 Dragan Tsankov Blvd., Sofia 1164, Bulgaria
salmonella.st@gmail.com

Abstract: The relationship between bacteriophages and antimicrobial resistance could be regraded in the scope of potential impact of microbiology on contemporary medicine and pharmaceuticals. Till now research projects have some ambiguous outcomes by confirming or examining the impact of the bacteriophages in variation of antimicrobial resistance genes. The major goal of our current study is to acquire a new knowledge how the viruses, their hosts and antimicrobial resistance genes are related and how this relationship can be clarified in the context of antimicrobial resistance dissemination through phages. The presented work is oriented towards zooming in the relationship and possible dependencies between bacteriophages and antimicrobial resistance. The data has been collected from different city environments all over the world. Our analyses consist of different bioinformatics and biostatistical methods for assessment of the differential abundance of phages, their diversity across samples, the impact on antimicrobial resistance categories and associations with antimicrobial resistant genes (ARGs) genes.

Keywords: Antimicrobial resistance, Bacteriophages diversity indexes, Relative risk, Compositional data analysis, Spatial analysis.

Acknowledgements: This work was partially supported by the financial funds allocated to the Sofia University "St. Kliment Ohridski", Grant No. 80-10-94/2022.

Hybrid Classification/Regression QSPR Modeling of Polyphenols' Antioxidant Activities in Stoichiometric and Kinetic Assays

Petko Alov [0000-0003-1320-2173], **Ivanka Tsakovska** [0000-0003-1389-1685], **Ilza Pajeva** [0000-0001-5412-1586]

Institute of Biophysics and Biomedical Engineering
Bulgarian Academy of Sciences
Acad. Georgi Bonchev Str., Bl. 105, Sofia 1113, Bulgaria
petko@biophys.bas.bg, pajeva@biomed.bas.bg,
itsakovska@biomed.bas.bg

Abstract: Plant polyphenols are considered responsible for the beneficial effects of fruits, vegetables, wines, and other foods of plant origin. These effects are primarily associated with modulation of the organism "redox state", thus polyphenols' interactions with free radicals are extensively studied. Quantitative structure-property relationships (QSPR) is a widely used methodology allowing not only to better understand the mechanisms of chemical reactions, including radical scavenging, but also to predict the relevant properties of chemical compounds without their synthesis, isolation and experimental testing. Modeling of the polyphenol antioxidants' activities in assays with stoichiometric endpoints (e.g., ABTS·+, DPPH·) depends strongly on the number of hydroxyl groups in their molecule. Here, we tested the feasibility of explicit classification of individual OH-groups as "active" or "inactive" in radical scavenging reactions and further use of the number of "active" OH-groups as a descriptor in simple-regression QSPR models. Modeling of the polyphenol antioxidants' activities in assays with kinetic endpoints (e.g., LA/ABAP·) relies on the selection of an OH-group in the molecule, either the "most reactive" one, or the one producing the "most stable phenoxyl radical" upon scavenging reaction in order to use electronic parameters of this OH-group in the model(s). Both cases pose a similar question, i.e., which electronic parameters pertinent to a single OH-group should we use in the classification: polyphenol molecule reactivity- or phenoxyl radical stability-related. The OH-groups were ranked by their reactivity- or stability-related electronic descriptors, either within a single molecule, in case of kinetic assays, or across the whole group of molecules, in case of stoichiometric assays. For the kinetic assays, the OH-group with the lowest classification parameter was selected. For the stoichiometric assays, a simple threshold classification based on the sum of TEAC (trolox-equivalent antiradical capacity) values was used for selection of "active" OH-groups. We showed that for both stoichiometric and kinetic assays, the regression models built on the "active" OH-groups' number or on the reactivity parameters of spin-density-classified OH-groups exhibit substantial improvement of statistical quality over the models employing enthalpy-classified OH-groups. This observation confirms that (i) phenoxyl radical stability plays a crucial role in both stoichiometric and kinetic antioxidant assays, and (ii) spin-density-related parameters reflect better the phenoxyl radical stability in polyphenols than bond dissociation enthalpies.

Keywords: Foods of plant origin, Antioxidant assays of polyphenols, QSPR, Classification/ regression modeling, Stoichiometric and kinetic endpoints, ABTS·+, DPPH·, LA/ABAP·, TEAC.

Acknowledgements: Funding from the Bulgarian Ministry of Education and Science under the National Research Programme “Healthy Foods for a Strong Bio-Economy and Quality of Life” (DCM #577/17.08.2018) is gratefully acknowledged.

Comparison of Docking Scoring Functions by InterCriteria Analysis on a Set of Protein Targets Related to Alzheimer and Parkinson Diseases

Petko Alov [0000-0003-1320-2173], **Ilza Pajeva** [0000-0001-5412-1586],
Ivanka Tsakovska [0000-0003-1389-1685], **Tania Pencheva** [0000-0003-1389-1685]

Institute of Biophysics and Biomedical Engineering
Bulgarian Academy of Sciences
Acad. Gorgi Bonchev Str., Bl. 105, Sofia 1113, Bulgaria
petko@biophys.bas.bg, itsakovska@biomed.bas.bg,
pajeva@biomed.bas.bg, tania.pencheva@biomed.bas.bg

Abstract: Nowadays, the pharmaceutical industry extensively uses *in silico* drug design to deal with the enormously wide chemical space of druggable compounds and to reduce the R&D expenses. Having a significant number of tools for structure-based *in silico* screening, the aim of this study was to assess the putative consonance between compound scorings with different docking programs, which could provide a basis for reduction of the screening computational cost and/or for optimal choice of scoring functions. The proteins used in the study were acetylcholine esterase (AChE), histone deacetylase 2 (HDAC2), and monoamine oxidase B (MAO-B), enzymes related to the treatment of symptoms of Alzheimer and Parkinson diseases and potential subjects for inclusion in "single drug – multiple targets" research. The 11 085 small molecules (ligands) used in the study were selected from a database of more than 600 000 commercially available drug-like compounds which docking scores obtained by a rigid docking were better than the re-docking scores of the cocrystalized reference ligands in the selected enzymes. To assess the differences in performance of the scoring functions implemented in different molecular docking software, docking of these ligands in the target proteins was performed using several widely used molecular modelling platforms: (i) rigid- and flexible-protein docking in MOE (v. 2019.01, https://www.chemcomp.com); (ii) rigid-protein docking in FlexX (v. 4.3) and ligand optimization and rescoring in HYDEscorer (v. 1.0), respectively (www.biosolveit.de); and (iii) rigid-protein docking in AutoDock Vina (https://vina.scripps.edu). Besides docking scores, the time for docking was also recorded and the computational costs were calculated for each of the studied docking protocol/scoring function pairs. The binding energies estimated by the selected scoring functions were subjected to intercriteria analysis (ICrA). The ICrA approach relies on the formalisms of the intuitionistic fuzzy sets and index matrices, and attempts to uncover similarities in the behavior of criteria applied for evaluation of multiple objects. ICrA was employed as a potential tool to support the selection of an appropriate scoring function for ranking of more than 11 000 ligands identified to interact with all three proteins simultaneously. Further, an analysis of the intersections of 2 the top 1000 ligands for each target ranked by different scoring functions, was performed. ICrA analysis revealed consonances between FlexX and AutoDock Vina scoring functions in

all studied proteins, and additionally between MOE flexible-protein docking and AutoDock Vina in AChE. Analysis of intersection results was to a great extent in line with the intercriteria relations. The results indicate that a precise selection of scoring functions and docking protocols, confirmed by the available knowledge of the studied objects, is needed. This analysis suggests also the possibility for optimization of *in silico* screening campaigns by avoidance of computationally expensive docking protocols that are highly consonant with the less expensive ones.

Keywords: Molecular docking, Scoring functions, Intercriteria analysis, Computational costs.

Acknowledgements: Funding from the National Science Fund of Bulgaria (Grants No. DN 17/6 and No. KP-06-OPR 03/8) is gratefully acknowledged.

Session

Mathematical Modelling in Biomedicine and Healthcare

Generalized Net Model of Rehabilitation Algorithm for Patients with Proximal Humeral Fracture after Surgical Treatment

Simeon Ribagin [1,2], **Antoaneta Grozeva** [2], **Stoyan Hristov** [3]

[1] *Department of Bioinformatics and Mathematical Modelling*
Institute of Biophysics and Biomedical Engineering
Bulgarian Academy of Sciences
Acad. Georgi Bonchev Str., Bl. 105, Sofia 1113, Bulgaria
simribagin@gmail.com
[2] *Department of Health and Pharmaceutical Care*
Medical College, "Prof. Dr. Assen Zlatarov" University
1 "Prof. Yakimov" Blvd., Burgas 8010, Bulgaria
antoaneta.grozeva@gmail.com
[3] *University Hospital Burgas, Burgas, Bulgaria*
hristov@dr.com

Abstract: The purpose of the present paper is to present an example of Generalized Nets application in orthopedics and traumatology rehabilitation. The model describes a possible algorithm protocol for rehabilitation treatment of the patients with fracture of the proximal humerus and the different transitions of the model are representing respectively the different parts of the rehabilitation process. The proposed model can be implemented in the decision making support systems, tele-rehabilitation platforms, optimization of the physiotherapy protocols for proximal humeral fractures rehabilitation based on current 'good practices' and better rehabilitation strategies.

Keywords: Proximal humeral fractures, Rehabilitation algorithm, Generalized Nets, GN-model.

Acknowledgements: The authors are grateful for the support provided by the University "Prof. Dr. Asen Zlatarov" – Burgas, Scientific research sector "Scientific and artistic activity" approved by No. NIH – 475 /2022 "Generalized nets models in orthopedic and traumatology rehabilitation".

Generalized Net Model of Density-based Spatial Clustering of Applications with Noise (DBSCAN) Algorithm and Its Application to a Diabetes Dataset

Petar Petrov [1,2], **Veselina Bureva** [1], **Janusz Kacprzyk** [3,4]

[1] *Laboratory of Intelligent Systems*
"Prof. Dr. Assen Zlatarov" University
1 "Prof. Yakimov" Blvd., Burgas 8010, Bulgaria
vbureva@btu.bg
[2] *Vocational School of Electrical Engineering and Electronics "Konstantin Fotinov"*
Burgas, Bulgaria
peshopbs2@gmail.com
[3] *Systems Research Institute, Polish Academy of Sciences*
6 Newelska Str., Warsaw 01-447, Poland
[4] *Warsaw School of Information Technology*
6 Newelska Str., Warsaw 01-447, Poland
kacprzyk@ibspan.waw.pl

Abstract: Density-based spatial clustering of applications with noise (DBSCAN) is a data science algorithm for density-based clustering. A Generalized net (GN) model of the DBSCAN algorithm is constructed. Intuitionistic fuzzy evaluations are defined to estimate the clustering procedure. The GN model of DBSCAN optimizes and estimates the procedure of the standard clustering algorithm. The clustering procedure is implemented using Python programming language. The method is then applied to a diabetes dataset to form clusters.

Keywords: Big data, Data mining, Machine learning, Data science, Generalized nets, Intuitionistic fuzzy sets.

Acknowledgements: The authors are thankful for the support provided by the European Regional Development Fund and the Operational Program "Science and Education for Smart Growth" under Contract UNITe No. BG05M2OP001-1.001-0004-C01 (2018-2023).

Generalized Net Model of the Malignant Melanoma Treatment

Evdokia Sotirova [1], **Hristo Bozov** [1,2], **Yaroslava Petrova** [1,2], **Greta Bozova** [3], **Krassimir Atanassov** [1,4]

[1] *"Prof. Dr. Assen Zlatarov" University*
1 "Prof. Yakimov" Blvd., Burgas 8010, Bulgaria
esotirova@btu.bg, hr_bozov@yahoo.com,
yaroslava_ap@abv.bg, k.t.atanassov@gmail.com
[2] *Oncology Complex Center – Burgas*
86 Demokratsiya Blvd., Burgas 8000, Bulgaria
[3] *Department of Nephrology, Military Medical Academy*
3 St. George Sofiiski, Sofia, Bulgaria
greti@abv.bg
[4] *Department of Bioinformatics and Mathematical Modelling*
Institute of Biophysics and Biomedical Engineering
Bulgarian Academy of Sciences
Acad. Georgi Bonchev Str., Bl. 105, Sofia 1113, Bulgaria

Abstract: In the paper, a generalized net model of the malignant melanoma treatment is proposed. Generalized nets are extension and generalization of the concept of Petri nets, as well as of other Petri nets extensions and modifications. For constructing of the model patients with malignant melanoma registered in Oncology Complex Center in Burgas town were analyzed. The model can be used as a uniform algorithm of behavior with patients with malignant melanoma from the initial examination to the treatment (if it is necessary).

Keywords: Generalized net, Malignant melanoma, Modelling.

Acknowledgements: The authors are thankful for the support provided by the European Regional Development Fund and the Operational Program "Science and Education for Smart Growth" under Contract UNITe No. BG05M2OP001-1.001-0004-C01(2018-2023).

Generalized Net Model of the Consequences of Earthquake

Stefka Fidanova [1], **Krassimir Atanassov** [2], **Leoneed Kirilov** [1],
Vanya Slavova [3], **Veselin Ivanov** [3]

[1] *Institute of Information and Communication Technologies*
Bulgarian Academy of Sciences
Acad. Georgi Bonchev Str., Bl. 25, Sofia 1113, Bulgaria
stefka.fidanova@gmail.com, l_kirilov_8@abv.bg
[2] *Bioinformatics and Mathematical Modelling Department*
Institute of Biophysics and Biomedical Engineering
Bulgarian Academy of Sciences
Acad. Georgi Bonchev Str., Bl. 105, Sofia 1113, Bulgaria
krat@bas.bg
[3] *Faculty of Medicine, Trakia University*
Stara Zagora 6000, Bulgaria
vslavova71@yahoo.com, veskoasenov@abv.bg

Abstract: In order to prevent victims of natural disasters and to be able to help the injured people, local medical authorities must be provided in advance. One of the worst natural disasters is strong earthquake. Therefore, it is good for decision makers to have a preliminary assessment of the possible consequences and injured people of earthquakes of various kinds. In this work we propose a model of the consequences of eventual earthquake and as well as the number and type of injured people. The model is based on the apparatus of Generalized Nets. After assessing the probability of an earthquake with a given intensity, a decision can be made on the necessary medical supplies to provide adequate assistance to the victims.

Keywords: Earthquake, Generalized nets, Model.

Acknowledgements: The authors are grateful to the Municipality of Stara Zagora and in particular to Eng. Veselin Kuzmanov for their advices. The work of Stefka Fidanova is supported by the Grant No. BG05M2OP011-1.001-0003, financed by the Science and Education for Smart Growth Operational Program and co-financed by European Union through the European structural and Investment funds and by National Scientific Fund of Bulgaria Grant No. DFNI KP-06-N52/5. The work of Leoneed Kirilov is supported by the Grant No. BG05M2OP011-1.001-0003, financed by the Science and Education for Smart Growth Operational Program and co-financed by European Union through the European structural and Investment funds and by National Scientific Fund of Bulgaria Grant No. DFNI KP-06-N52/7. The work of Veselin Ivanov and Vanya Slavova is supported by Project 9/2019 of Medical Faculty, Trakia University, Stara Zagora 6000, Bulgaria.

A Generalized Net Model of Time-Delay Recurrent Neural Networks with the Stochastic Gradient Descent and Dropout Algorithm

Plamena Yovcheva [1], **Sotir Sotirov** [1], **Vanya Georgieva** [1], **Radovesta Stewart** [1], **Maciej Krawczak** [2]

[1] *Intelligent Systems Laboratory*
"Prof. Dr. Assen Zlatarov" University
Burgas 8010, Bulgaria
plamena.iovcheva@abv.bg, ssotirov@btu.bg,
v.kr.georgieva@gmail.com, radadeva@yahoo.com
[2] *Warsaw School of Information Technology*
6 Newelska Str., Warsaw 01-447, Poland
[3] *Systems Research Institute, Polish Academy of Sciences*
6 Newelska Str., Warsaw 01-447, Poland
krawczak@ibspan.waw.pl

Abstract: Tapped delay lines and recurrent connections are two different components that are used along to design a time-delay recurrent neural network with a stochastic gradient descent algorithm in combination with a dropout method.

Keywords: Dropout algorithm, Generalized net, Neural network, Stochastic gradient descent algorithm, Time-delay Recurrent neural network.

Acknowledgements: The authors are thankful for the support provided by the European Regional Development Fund and the Operational Program "Science and Education for Smart Growth" under Contract UNITe No. BG05M2OP001-1.001-0004-C01(2018-2023).

Generalized Net Model of the Vegetative (Autonomic) Innervation of Gastrointestinal Tract

Valentina Ignatova [1], **Krassimir Atanassov** [2,3]

[1] *Clinic of Neurology, National Cardiology Hospital*
65 Konyovitsa Str., Sofia 1309, Bulgaria
valyaig@abv.bg
[2] *Intelligent Systems Laboratory, "Prof. Dr. Assen Zlatarov" University*
1 "Prof. Yakimov" Blvd, Burgas 8010, Bulgaria
k.t.atanassov@gmail.com
[3] *Department of Bioinformatics and Mathematical Modelling*
Institute of Biophysics and Biomedical Engineering
Bulgarian Academy of Sciences
Acad. Georgi Bonchev Str., Bl. 105, Sofia 1113, Bulgaria
krat@bas.bg

Abstract: The gastrointestinal tract (GIT) is a basic part of the human body. It interacts with many organs and systems and has a complex autonomic innervation. Generalized net model of GIT innervation is described and the relations with central nervous system are shown. Some applications of the model are discussed.

Keywords: Gastrointestinal tract, Generalized net, Human body, Innervation.

Acknowledgements: The authors are thankful for the support provided by the European Regional Development Fund and the Operational Program "Science and Education for Smart Growth" under Contract UNITe No. BG05M2OP001-1.001-0004-C01(2018-2023).

A Generalized Net Model of the Prostate Cancer Early Stages of Development

Elenko Popov [1,2], **Radostina Georgieva** [1,2], **Dmitrii Dmitrenko** [1,2], **Borislav Bojkov** [1,2], **Chavdar Slavov** [1,2], **Martin Lubich** [3], **Peter Vassilev** [4], **Vassia Atanassova** [4], **Lyudmila Todorova** [4], **Krassimir T. Atanassov** [4]

[1] *Faculty of Medicine, Medical University of Sofia*
15 Acad. Ivan Geshov Blvd., Sofia 1431, Bulgaria
shennyp@yahoo.com (E.P.), rgeorgieva50@gmail.com (R.G.),
dmitrii.dmitrenko@gmail.com (D.D.), b.b.bojkov@gmail.com (B.B.),
ch.k.slavov@gmail.com (C.S.)
[2] *Department of Urology and Andrology*
University Hospital Tsaritsa Yoanna – ISUL
8 Byalo More Str., Sofia 1527, Bulgaria
[3] *Department of Nephrology, University Hospital Sofiamed*
16 G. M. Dimitrov Blvd., Sofia 1797, Bulgaria
martinlub11@abv.bg (M.L.)
[4] *Department of Bioinformatics and Mathematical Modelling*
Institute of Biophysics and Biomedical Engineering
Bulgarian Academy of Sciences
Acad. Georgi Bonchev Str., Bl. 105, Sofia 1113, Bulgaria
peter.vassilev@gmail.com (P.V.), vassia.atanassova@gmail.com (V.A.),
lpt@biomed.bas.bg (L.T.), krat@bas.bg (K.A.)

Abstract: A generalized net model of the prostate cancer early stages of development is described. The relationship of the prostate with the human body respiratory, blood and circulatory, and endocrine systems are represented.

Keywords: Generalized net, Model, Prostate cancer.

Acknowledgements: This research is supported by the Bulgarian National Science Fund under Grant No. KP-06-N43/7 “Creating a prognostic model predicting life expectancy in prostate cancer patients and providing better quality of life after definitive surgical treatment” from 30.11.2020.

Session

Biomedical Approaches and Applications

Urocortin 3 in the Posterodorsal Medial Amygdala Mediates Stress-induced Suppression of LH Pulsatility in Female Mice

Deyana Ivanova [1], Xiao-Feng Li [1], Caitlin McIntyre [1], Yali Liu [2], Lingsi Kong [1], Kevin T. O'Byrne [1]

[1] *Department of Women and Children's Health, Faculty of Life Science and Medicine, King's College, London, United Kingdom; deyana.ivanova@kcl.ac.uk*
[2] *Department of Assisted Reproduction, Shanghai Ninth People's Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, People's Republic of China*

Abstract: Psychosocial stress disrupts reproduction and interferes with pulsatile luteinizing hormone (LH) secretion in mammals. The posterodorsal medial amygdala (MePD) is an upstream modulator of the hypothalamus pituitary gonadal (HPG) and hypothalamus pituitary adrenal (HPA) axis. Psychosocial stress exposure alters urocortin3 (Ucn3) and its receptor corticotropin-releasing factor type-2 receptor (CRFR2) activity within the MePD. We began by investigating whether Ucn3 signalling in the MePD is involved in mediating the effect of psychosocial stress on LH pulsatility and corticosterone (CORT) secretion in adult female mice. We administered Ucn3 into the MePD and we delivered Astressin2B, a selective CRFR2 antagonist, intra-MePD in the presence of predator odor, 2,4,5-Trimethylthiazole (TMT) whilst examining the effect on LH pulses in C57Bl6/J female adult ovariectomised mice. We then virally infected Ucn3-cre-tdTomato female adult ovariectomised mice with inhibitory designer receptors exclusively activated by designer drugs (DREADDs) targeting MePD Ucn3 neurons during TMT or restraint stress exposure to examine the effect on LH pulsatility and CORT release. We found that administration of Ucn3 into the MePD dose-dependently inhibits LH pulses and Astressin2B blocks the suppressive effect of TMT on LH pulsatility whilst inhibition of MePD Ucn3 neurons blocked TMT and restraint stress-induced suppression of LH pulses and CORT release. These results demonstrate for the first time that Ucn3 neurons in the MePD mediate psychosocial stress-induced suppression of the GnRH pulse generator and CORT secretion. We then unilaterally injected AAV-ChR2 and implanted optofluid cannulae targeting the MePD in adult Ucn3-cre-tdTomato female ovariectomised mice. We stimulated Ucn3 neurons in the MePD with blue light at 10 Hz, 10 mW and monitored the effect on LH pulses. Then combining optogenetic stimulation of MePD Ucn3 neurons with pharmacological antagonism of GABAA, GABAB, NMDA and AMPA receptors with bicuculline, CGP or a cocktail of AP5 and CNQX, respectively, we observed the effect on pulsatile LH secretion. Additionally, in a separate group of Ucn3-cre-tdTomato female ovariectomised mice with oestradiol replacement we optically stimulated MePD Ucn3 efferent projections in the hypothalamic paraventricular nucleus (PVN) with blue light at 20 Hz, 15 mW and monitored the effect on CORT secretion and pulsatile LH secretion. We reveal that activation of local Ucn3 neurons in the MePD inhibits GnRH pulse generator activity via GABA and glutamate neurotransmission within the MePD and Ucn3 efferent projections from the MePD to the PVN modulate the HPG and HPA axis. MePD Ucn3 neurons may represent a nodal centre in the interaction between the reproductive and stress axes.

Relation between Oxidative Stress and Morphometric Alterations of Red Blood Cells Derived from Women with Early Pregnancy Loss

Ariana Langari [1], **Velichka Strijkova** [1,2], **Avgustina Danailova** [1], **Sashka Krumova** [1], **Stefka G. Taneva** [1], **Ina Giosheva** [1,3], **Tania Stoyanova** [1], **Lora Topalova** [1], **Regina Komsa-Penkova** [4], **Svetla Todinova** [1]

[1] *Institute of Biophysics and Biomedical Engineering*
Bulgarian Academy of Sciences
Acad. Georgi Bonchev Str., Bl. 21, Sofia 1113, Bulgaria
arianalangari@abv.bg (A.L.), avgustina_danailova@abv.bg (A.D.), sashka.b.krumova@gmail.com (S.K.), sgtaneva@gmail.com (S.G.T.), tanya.sttoyanova@gmail.com (T.S.), topalovaloram@gmail.com (L.T.), todinova@abv.bg (S.T.)

[2] *Institute of Optical Materials and Technologies*
Bulgarian Academy of Sciences, Sofia
vily_strij@abv.bg

[3] *University Obstetrics and Gynecology Hospital "Maichin Dom"*
2 Zdrave Str., Sofia 1463, Bulgaria
ina_gi@abv.bg

[4] *Department of Biochemistry, Medical University*
1 St. Kliment Ohridski Str., Pleven 5800, Bulgaria
rkomsa@gmail.com

Abstract: Early pregnancy loss (EPL) is estimated to occur in 10–15% of all clinically recognized pregnancies. Oxidative stress is known to be involved in the pathophysiology of various pregnancy complications, including EPL.Herein, we apply optical and atomic force microscopy (AFM) to assess the changes in red blood cells (RBCs) morphology from EPL patients compared to healthy pregnant (PC) and not pregnant women (NPC) and relate the occurrence of oxidative stress to these transformations.The morphology of freshly isolated EPL RBCs was not significantly different from that of NPC and PC with biconcave cells dominating. However, freshly prepared cells from women with EPL differed in membrane roughness value compared to those of NPC and PC. We find a time-dependent trend in decreasing cell size and surface roughness, which is much faster for EPL than for both control groups. Accelerated aging of EPL erythrocytes is also expressed in an earlier morphological shape transformation. Induction of oxidative stress by hydrogen peroxide on freshly isolated healthy RBCs resulted in a significant reduction of cells with normal shape and functionality (i.e., biconcave RBCs) at the expense of those with reduced functionality (spiculocytes and spherocytes). These alterations mimic the morphological changes that occurred in EPL RBCs during cells' aging. In summary, the obtained results lead to the conclusion that the aging of erythrocytes in the EPL group occurs at an earlier stage compared to the control groups and that this effect is likely to be due to the susceptibility of the cells to oxidative stress.

Keywords: Erythrocytes, Early pregnancy loss, Atomic force microscopy, Optical microscopy, Cell aging, Oxidative stress.

Acknowledgements: This work is supported by Grant No. КП-06-Н21/4, Competition for financial support for basic research projects – 2018, National Science Fund. The equipment of the Distributed Scientific Infrastructure INFRAMAT, part of the National Roadmap of Bulgaria for Scientific Infrastructure, financially supported by the Ministry of Education and Science, was used in these studies.

Methods of Treatment of Congenital Deformities of the Musculoskeletal System: *Talipes equinovarus*

Maria Dragomirova, Marina Yaneva

Faculty of Medicine, University "Prof. D-r Assen Zlatarov"
Burgas 8010, Bulgaria
maria5k@abv.bg, marinaiaaneva@abv.bg

Abstract: *Talipes equinovarus*, also called clubfoot, is characterized by plantar flexion, inward tilting of the heel (from the midline of the leg), and adduction of the forefoot (medial deviation away from the leg's vertical axis). Idiopathic congenital *Talipes equinovarus* is the most common pediatric deformity and occurs in 1 in every 1000 live births. Even though it has been widely researched, the etiology of the condition remains poorly understood and is often described as being based on different factors. Genetic and environmental factors seem to have a major role in the development of this disease. If left untreated, it can result in long-term disability, deformity and pain. Interventions can be conservative (such as splinting or stretching) or surgical. Prenatal screening is key as treatment usually begins days after birth. Typical management of *Talipes equinovarus* is non-operative and utilizes serial manipulation and casting, followed by bracing with Ponseti method. For cases unresponsive to the conservative methods, a variety of surgical approaches is used to address the deformity and sustain a full correction of the musculoskeletal system. A key point for full recovery is the utilization of intensive physiotherapy in the posttreatment period. We follow the case of a male patient, who was diagnosed with *Talipes equinovarus* prenatally and observe his non – surgical and surgical treatment over the course of 28 months, which resulted in full recovery.

Keywords: *Talipes equinovarus*, Ponseti method, Clubfoot.

Identification of Antioxidant and Immunomodulating Metabolites in the Leaves of the Endemic Plant *Haberlea rhodopensis* Friv.

Yordan Nikolaev Georgiev [1, [0000-0002-3988-3256], *], **Gabriela Asenova Fazlova** [2], **Petko Nedyalkov Denev** [1, [0000-0002-2290-791X]], **Christian Winther Wold** [3, [0000-0002-3967-3849]], **Ondrej Vasicek** [4, [0000-0001-5892-0457]], **Irina Zheleva Yanakieva** [1], **Balik Malomirov Dzhambazov** [5, [0000-0001-8052-5840]], **Tsvetelina Georgieva Batsalova** [5, [0000-0002-6560-1945]], **Desislava Georgieva Teneva** [1, [0000-0003-3109-2238]], **Manol Hristov Ognyanov** [1, [0000-0002-5568-0854]], **Daniela Ivanova Pencheva** [1, [0000-0002-9367-8448]], **Kari Tvete Inngjerdingen** [3, [0000-0002-0266-9862]], **Berit Smestad Paulsen** [3, [0000-0003-4099-1083]], **Albert Ivanov Krastanov** [2, [0000-0003-2794-1655]]

[1] *Laboratory of Biologically Active Substances*
Institute of Organic Chemistry with Centre of Phytochemistry
Bulgarian Academy of Sciences
139 Ruski Blvd., Plovdiv 4000, Bulgaria
yordan.georgiev@orgchm.bas.bg, petko.denev@orgchm.bas.bg, irina.yanakieva@gmail.com, desislava.teneva@orgchm.bas.bg, manol.ognyanov@orgchm.bas.bg, daniela.klisurova@orgchm.bas.bg
[2] *Department of Biotechnology, University of Food Technologies*
26 Maritza Blvd., Plovdiv 4002, Bulgaria
gabriela_fazlova@abv.bg, a_krastanov@uft-plovdiv.bg
[3] *Department of Pharmacy, University of Oslo*
P. O. Box 1068 Blindern, 0316 Oslo, Norway
christianwintherwold@gmail.com, k.t.inngjerdingen@farmasi.uio.no, b.s.paulsen@farmasi.uio.no
[4] *Department of Biophysics of Immune System*
Institute of Biophysics, Czech Academy of Sciences
135 Kralovopolska Str., Brno 612 65, Czech Republic
ondrej.vasicek@ibp.cz
[5] *Department of Developmental Biology*
Plovdiv University Paisii Hilendarski
24 Tsar Assen Str., Plovdiv 4000, Bulgaria
balik@uni-plovdiv.bg, tsvetelina@uni-plovdiv.bg
* *Corresponding author*

Abstract: The study aimed to characterize the chemical composition of an aqueous polysaccharide-rich extract (PSE) from the leaves of *H. rhodopensis*, and to identify some of its antioxidant and immunomodulatory constituents. PSE (yield: 28.5%) contained 25.7% total phenolics, of which 1.2% total lignins, 3.5% phenolic acids, and 3.7% flavonoids were elucidated. It was also composed of 4.4% water-soluble PSs (WSPSs-PSE), free sugars (21.0%) and organic acids (8.3%). WSPSs-PSE contained 89.4% total carbohydrates, including 27.7% uronides, and 5.0% phenolics and 2.2% proteins. WSPSs-PSE contained highly methyl-esterified and low-acetylated homogalacturonan-rich pectins with smaller amounts of rhamnogalacturonan (RG) type I and II. These pectins activated the oxidative burst from human whole blood phagocytes in a dose-dependent manner (50-200 μg/mL) *ex vivo*. They elevated T cell, NK cell, and granulocyte counts from peripheral blood. The RG-I fractions, enriched with α-L-arabino-3,6-β-D-galactans, were responsible for the immunostimulating activity on murine macrophages *in vitro*. The co-stimulation with

RG-I fractions and IFN-γ induced high NO production in macrophages even at a concentration of 0.39 μg/mL. This suggested recognition of PSs via toll-like receptors. The ORAC and HORAC antioxidant activities of PSE were 9505.5 TE/g and 978.7 GAE/g, respectively. Although 90% of the phenolics in PSE were extracted with 70% ethanol, the coagulated WSPSs-PSE retained potent ORAC (52173.3 TE/g) and HORAC (17774.3 GAE/g) activities. Myconoside bound to pectins was suggested to contribute to the antioxidant activity of WSPSs-PSE, but neither tannins nor lignins. Therefore, the co-extraction of PSs with phenolics can lead to development of beneficial products with improved bioactivities.

Keywords: *Haberlea rhodopensis*, Polysaccharides, Polyphenols, Immunomodulating activity, Antioxidant activity.

Acknowledgements: This study was funded by the Program for support of young scientists and doctoral students in the Bulgarian Academy of Sciences – 2017, Grant No. DFNP-17-62/July 26, 2017 and by the Bilateral grant agreement between the Bulgarian Academy of Sciences and Czech Academy of Sciences (2020-2022).

Rehabilitation Approach after Arthroscopic Rotator Cuff Repair

Gergana Angelova-Popova

Department of Health and Pharmaceutical Care, Medical College
University "Prof. D-r Assen Zlatarov"
Burgas 8010, Bulgaria
giggi_popa@abv.bg

Abstract: Rotator cuff tears are often the cause of incapacitating shoulder pain, reduced shoulder function, and compromised joint mechanics with clinical manifestations of shoulder stiffness, weakness, instability and limitation of daily activities. The arthroscopic approach is increasingly used due to potential benefits such as minimal invasiveness, less postoperative pain while allowing secure fixation and early return of range of motion. Although arthroscopic rotator cuff repair appears to be a relatively mild procedure, postsurgical rehabilitation is critical in terms of long-term recovery of the reconstructed tendons. The main goal of rehabilitation after rotator cuff tear is to reduce the stress on the operated tissues and improve their healing, while preventing muscle stiffness and atrophy.

Keywords: Rotator cuff tears, Physical therapy, Rehabilitation, Shoulder.

Acknowledgements: The author is grateful for the support provided by the University "Prof. Dr. Assen Zlatarov" – Burgas, Scientific research sector "Scientific and artistic activity" approved by No. NIH – 475 /2022 "Generalized nets models in orthopedic and traumatology rehabilitation".

Stress Response of Gram-Positive and Gram-Negative Bacteria Induced by Metal and Non-Metal Nanoparticles. In Search of Smart Antimicrobial Agents

Iliana Ivanova [1], Radostina Toshkovska [1], Lyubomira Yocheva [2], Dayana Benkova [3], Vesela Yordanova [3], Alexandrina Nesheva [3], Rusina Hazarosova [3], Galya Staneva [3,*], Aneliya Kostadinova [3,*]

[1] *Sofia University "St. Kliment Ohridski", Faculty of Biology*
8 Dragan Tzankov Blvd., Sofia 1164, Bulgaria
[2] *Sofia University "St. Kliment Ohridski", Faculty of Medicine*
1 Koziak Str., Sofia 1407, Bulgaria
[3] *Institute of Biophysics and Biomedical Engineering, Bulgarian Academy of Sciences*
Acad. Georgi Bonchev Str., Bl. 21, Sofia 1113, Bulgaria
[*] gstaneva@obzor.bio21.bas.bg, aneliakk@yahoo.com

Abstract: Because of increasing resistance of pathogenic bacteria to commercially available antibiotics, the attention of the scientific community in the last decades is focused on the study of various nanotechnology products as an alternative to antibiotics and more effective antimicrobial agents.

The aim of this work was to study the effects of nanomaterial dispersions as Selenium (Se), Gold (Au), Iron oxide (Fe_2O_3), Silicon dioxide (SiO_2) and Graphene oxide (GO) on bacteria like *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Bacillus cereus* and two strains of *Escherichia coli*. Two classical methods were used to investigate the antibacterial effect of the nanoparticles (NPs): Spot and Well diffusion tests in agar medium. The tested nanoparticles were active against Gram-positive bacteria in concentrations between 3.0 and 1.5 µg/mL but they were not active against Gram-negative bacteria such as *E. coli*. Among tested nanomaterials, SeNPs express the strongest antimicrobial effect. Gold nanoparticles with Polyvinylpyrrolidone (Au-PVP NPs) were more active against bacteria than pure AuNPs. Lower concentrations (1.0 mg/mL and 0.5 mg/mL) of Se, GO and the two types of Gold nanoparticles did not show activity against all test microorganisms. Fe_2O_3 NPs as well as SiO_2 NPs had no effect on any test bacteria in the mentioned concentrations.

In conclusion, the most cytotoxic for tested bacteria were SeNPs, followed by Au-PVP and AuNPs. GONPs also showed a certain cytotoxic effect, especially on *B. cereus* 1095.

Keywords: Antimicrobial effect, Nanoparticles, Gram-positive bacteria, Gram-negative bacteria.

Acknowledgements: This study was financially supported from the National Science Fund of Bulgaria by Grant КП-06-Н58/6-19.11.2021. The authors thank the Bulgarian Ministry of Education and Science for support: Scientific Infrastructure on Cell Technologies in Biomedicine (SICTB) DO1-154/28/08/2018 and D01-392/2020 "National Center for Biomedical Photonics", part of Bulgarian National Roadmap for Scientific Infrastructures 2020-2027.

Lipid Order of Membranes Isolated from Erythrocytes of Patients with Coronary Artery Disease: Correlation with Biochemical Parameters

Vesela Yordanova [1,*,‡], **Galya Staneva** [1,*,‡], **Plamen Krastev** [2], **Tania Markovska** [1], **Ana-Mariya Marinovska** [1], **Aneliya Kostadinova** [1], **Rusina Hazarosova** [1], **Albena Momchilova** [1]

[1] *Institute of Biophysics and Biomedical Engineering*
Bulgarian Academy of Sciences
Acad. Georgi Bonchev Str., Bl. 21, Sofia 1113, Bulgaria
vyordanova@biophys.bas.bg, gstaneva@bio21.bas.bg, markovska@abv.bg, anamariya.walter@gmail.com, aneliakk@yahoo.com, r_hazarosova@abv.bg, albena_momchilova@abv.bg

[2] *Cardiology Clinic, University Hospital "St. Ekaterina"*
52A P. Slaveykov Blvd., Sofia 1431, Bulgaria
plamenkr@mail.bg

[*] *Corresponding authors*

[‡] *Both authors contributed equally to this work*

Abstract: Coronary artery disease (CAD) is a medical condition that is characterized by an inability of the arteries to supply the myocardium of the heart with enough blood, therefore affecting its function and leading to serious pathological changes. CAD development is caused by plaque buildup on the inner walls of the coronary arteries. The plasma and red blood cell lipids are involved in plaque formation. In this study, the fatty acid (FA) composition was determined in blood plasma and membranes isolated from erythrocytes of treated patients against CAD and healthy controls. Higher saturated/unsaturated FA ratio was found in the erythrocyte ghost membranes of patients compared to controls.

Moreover, the triglyceride (TG) levels of CAD patients were also higher compared to the control group. No difference in total cholesterol and LDL-cholesterol levels was observed between patients and control group.

Unexpectedly, despite the observed higher level of saturated FAs in the erythrocyte membranes, lower membrane lipid order was found for CAD group compared to the control one. Our results suggest that the serum TGs govern more significantly the lipid order of CAD ghost membranes than the saturated/unsaturated FA ratio. This finding is in accordance with the literature data stating an inverse relationship between TG levels and the lipid anisotropy in model and erythrocyte membranes. The present study implies that CAD treatment is able to decrease erythrocyte membrane lipid order, whereas higher levels of TGs in blood serum and saturated FAs in erythrocyte membranes still represent a critical potential risk for CAD patients compared to healthy individuals.

Keywords: Blood plasma, Erythrocyte ghosts, Fatty acids, Lipid profile, Membrane lipid order.

Acknowledgements: This study was financially supported from the National Science Fund of Bulgaria by Grant No. КП-06-Н58/6-19.11.2021. The authors thank the Bulgarian Ministry of Education and Science for support: Scientific Infrastructure on Cell Technologies in Biomedicine (SICTB) DO1-154/28/08/2018 and D01-392/2020 "National Center for Biomedical Photonics", part of Bulgarian National Roadmap for Scientific Infrastructures 2020-2027. The authors also acknowledged COST Action 17 121: Correlated Multimodal Imaging in Life Sciences – COMULIS by Grant No. KP-06-COST/10/2020.

Phytochemical Composition and Therapeutic Potential of *Bistorta major* Gray: A Review

Yordan Georgiev [*,[0000-0002-3988-3256]], **Manol Ognyanov** [0000-0002-5568-0854], **Petko Denev** [0000-0002-2290-791X]

Institute of Organic Chemistry with Centre of Phytochemistry
Bulgarian Academy of Sciences
139 Ruski Blvd., 4000 Plovdiv, Bulgaria
yordan.georgiev@orgchm.bas.bg; *manol.ognyanov@orgchm.bas.bg*;
petko.denev@orgchm.bas.bg
* *Corresponding author*

Abstract: *B. major* is an edible medicinal plant, which aqueous and hydroethanolic rhizome extracts are used in folk medicine for the relief of diarrhea and more gastrointestinal disorders, hemorrhages, inflammations, respiratory and other infections, wounds, etc. The progress on the bistort extract research enables the discovery of new bioactive compounds, evaluation of their therapeutic potential and safety for the treatment of modern socially significant diseases. Therefore, the present review aimed to analyze the therapeutic potential of *B. major* extracts with an emphasis on their active molecules, and the toxicological risk of bistort use. The antioxidant phenolics are among the most investigated phytochemicals in the plant, as two new flavonoids with anti-inflammatory properties have been discovered. The herb is a source of chlorogenic, gallic acids, catechins, procyanidins, and derivatives of caffeic acid, quercetin, kaempferol, luteolin and apigenin. Some triterpenoids, phenolic acids, flavan-3-ols, flavonols, tannins, and fatty acids are among the elucidated physiologically active compounds in the extracts. They are responsible for their antibacterial, antioxidant, hemostatic, immunostimulatory, anti-inflammatory, hepatoprotective, gastroprotective, and anticancer effects. Particularly, 5-glutinen-3-one and tannic acid are promising anti-rheumatic and hepatoprotective agents, respectively. However, the role of polysaccharides in the bioactivity of the aqueous extracts is not studied. It seems that by decreasing the polarity of the extragent it can increase the possible toxic effects of the extract on the basis of toxicological studies. Considering the biological and pharmacological investigations with bistort extracts, their biomedical potential deserves to be tested in malignant, infectious, chronic inflammatory, liver, gastrointestinal, cardiovascular diseases and diabetes

Keywords: *Bistorta major*, Bistort, Phytochemistry, Phenolics, Biological activity, Biomedicine, Nutrition.

Reactivity of Recombinant and Native pLDH Antigens with Seven Commercially Available Rapid Diagnostic Test Kits for Malaria Diagnosis

Daniela Todorova-Balvay [1,‡], **Ravishankaran R.** [2,‡], **Pillai C. R.** [3], **Xavier C. Ding** [4], **Desai P. K.** [1,2,*]

[1] *Span Diagnostics SARL, Parc Technologique des Rives de l'Oise*
Rue les Rives de l'Oise, BP 50149 Venette – 60201 Compiegne Cedex France
contact@span-diagnostics.com, pradipk.desai@gmail.com
[2] *Span Bioproducts Pvt. Ltd*
9th Floor, Rajhans Bonista, Ghod-Dod Road, Surat 395001, India
jairavibt@gmail.com, pradipk.desai@gmail.com
[3] *Indian Council of Medical Research,*
National Institute of Malaria Research
Sector 8, Dwarka, New Delhi 110077, India
pillaicr@rediffmail.com
[4] *Foundation for Innovative New Diagnostics (FIND)*
Campus Biotech, 9 Chemin des Mines
Geneva 1202, Switzerland
xavier.ding@gmail.com
[*] *Corresponding author*
[‡] *Both authors have equal contribution*

Abstract: *Purpose:* The glycolytic enzyme, lactate dehydrogenase (LDH), is a widely used diagnostic marker for malaria caused by *Plasmodium* species. Each *Plasmodium* species has a unique genetic sequence for LDH; this can be used to construct species-specific antigens for validation of rapid diagnostic tests (RDTs) for malaria. This study aims to review seven RDTs widely used in India for the sensitivity and specificity of *Plasmodium falciparum* and non-*falciparum* species based on *Plasmodium* LDH pLDH test bands.

Methods: Out of seven, four RDTs detect *P. vivax* specifically, while the remaining three are pan-malaria reactive. RDTs were evaluated using six species-specific recombinant pLDH antigens and the native LDH antigens present in the clinical blood samples of *in vitro* cultures of *P. falciparum* and *P. vivax*.

Results: First Response RDT showed high sensitivity and specificity followed by FalciVax with good sensitivity and *P. vivax* species specificity. ParaHIT and SD BIOLINE RDTs reacted only with *P. ovale wallikeri* but not with *P. ovale curtisi*, while TRUSTline and First Response were able to detect recombinant *P. ovale* (both subspecies). None of the kits detected *P. malariae*/*P. knowlesi* recombinant pLDHs.

Conclusion: Our analysis of non - *P. falciparum* (Pf) / *P. vivax* (Pv) species detection alongside Pf/Pv species detection shows the shortcomings of currently usable RDTs and emphasises the importance of RDT enhancement. To the best of our knowledge, our study is

the first to compare the efficacy of commercially available RDTs in India; this highlights the need to create higher specificity malarial diagnostic kits".

Keywords: Lactate dehydrogenase, *P. falciparum*, *P. vivax*, *Plasmodium* species, RDTs.

Acknowledgements: We acknowledge the help of SRKRC in providing the clinical samples used in this study. We thank Dr Ramya Ramachandran, Scientist at Span Bioproducts Pvt. Ltd., for compiling the data and writing the original draft of the manuscript; Shukla Maitri and Thakur Angira, Research Assistants at Span Bioproducts Pvt. Ltd., for their involvement in culturing *P. falciparum* and *P. vivax* and for performing tests of the RDTs. We also thank Dr.Walid Yakoub and Mrs. Sandra Dirson of Span Diagnostics SARL, France, for preparing the recombinant antigens used in this study. We thank Assoc. Prof. Dr. Milen Todorov, "Prof. Dr. Assen Zlatarov" University, Burgas, Bulgaria for the informatic expertise.