

#BelBi2023 • Belgrade, Serbia

BOOK OF ABSTRACTS



4th Belgrade Bioinformatics Conference

HYBRID • 19 - 23 JUNE 2023

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ISBN: 978-86-82679-14-1

belbi.bg.ac.rs

Title	4 th Belgrade Bioinformatics Conference BOOK OF ABSTRACTS
Publisher	Institute of Molecular Genetics and Genetic Engineering, University of Belgrade Vojvode Stepe 444a, Belgrade, Serbia https://www.imgge.bg.ac.rs/
Editors	dr. Ivana Morić dr. Valentina Đorđević
Technical editor	Dušan Radojević
ISBN	978-86-82679-14-1
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FOREWORD

Dear colleagues and friends,

The 4th Belgrade Bioinformatics Conference - BelBi2023, where many high-quality scientific contributions were presented, has just ended. With great thanks to all participants, we now proudly present a book of abstracts that both reflects the scientific abundance and diversity of the conference and serves as a reminder of a memorable event.

Several research institutions, faculties, and scientific societies from Serbia joined forces in organizing this international conference, which covered numerous topics in computational biology, bioinformatics, and biomedical and health informatics. The main goal of BelBi2023 was to foster contact between scientists, both early stage career and senior researchers, allowing them to share experiences and latest advances in their fields. We sincerely hope that BelBi2023 has served as a platform for researchers from around the world to meet, initiate new collaborations, and expand professional contacts, and that all of you would become a part of the growing BelBi community.

We are grateful and proud to have welcomed more than 250 researchers from 21 countries. We have had 28 scientific sessions, consisting of more than 60 lectures (including eight Keynote talks), 47 presented posters, as well as three workshops and one satellite event – COST action. We have also organized seven industry lectures, including the NGS Challenge,

two Meet the Expert Sessions, and one Business Coffee Break where ten start-up companies took part. And finally, the future BIO4 campus was presented and first panel on Serbia's resources for storage and analyses of genetic data was organized.

We would like to thank all the members of the International Advisory Board and the International Program Committee for their efforts and help in making this event a success. We are very grateful to the Ministry of Science, Technological Development and Innovation of the Republic of Serbia, SAIGE project, and UNDP-Serbia for their support. Finally, the Local Organizing Committee is very grateful to all the sponsors of the conference - BGI, Illumina & Elta'90MS, PacBio & East Diagnostics, ThermoFisher Scientific & Vivogen, Huawei, Labena, DSP Chromatography, RNIDS, Telekom Srbija, Alfa Genetics, Kefo and Superlab, hoping that they will stay with us for many years to come.

Looking forward to seeing you again at the 5th Belgrade Bioinformatics Conference.

Belgrade, July 2023

Dr. Valentina Đorđević
& *Dr. Ivana Morić,*
On behalf of BelBi2023
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Oral presentation

Modulating Horizontal Gene Transfer through Bistability in the Dynamics of Bacterial Restriction-Modification Systems

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Restriction-modification (R-M) systems consist of genes encoding restriction enzyme and methyltransferase, often co-expressed with a specialized regulator (C protein). These systems tightly regulate their function through complex cooperative positive and negative feedback loops. R-M systems defend bacterial cells against invasion by foreign DNA, such as plasmids and bacteriophages, consequently modulating horizontal gene transfer, including transmitting pathogenic genes like antibiotic resistance determinants or virulence factors. Recent experiments have directly confirmed that the R-to-M ratio significantly impacts bacteriophage infection efficiency, rendering a subset of cells more susceptible to horizontal gene transfer.

To understand the regulatory mechanisms of R-M systems, we develop a mathematical model tightly constrained by biophysical measurements of system interaction parameters. Despite the technical complexity arising from C protein forming dimer and tetramer complexes, we analytically derive a system stability diagram that can be easily modified for various R-M system architectures. A single free parameter determines the bistability of the system, which we infer from experimental measurements across three different architectures. Surprisingly, while one class exhibits monostability, the other two demonstrate bistability.

Our model successfully explains the experimental data and reveals that modulation of the barrier to horizontal gene transfer can occur through distinct mechanisms. Bistability leads to long-lasting states susceptible to acquiring pathogenic genes, whereas stochastic fluctuations only transiently lower the transfer barrier. The precise implications of these differences for bacterial pathogenicity and evolution require further investigation. However, we propose that R-M systems capable of bistable gene expression may give rise to genetically distinct bacterial populations with potentially diverse phenotypes concerning pathogenicity and antibiotic resistance.

Keywords: restriction-modification systems, nonlinear dynamics modeling, biophysical modeling, bistability, antibiotic resistance

Acknowledgments: This work is supported by The Science Fund of the Republic of Serbia (Grant no. 7750294, q-bioBDS).



ISBN: 978-86-82679-14-1