OPINION

on the materials submitted for the competition for the academic position of Associate Professor, in the professional field 4.3. Biological Sciences, scientific specialty Molecular Biology, announced in the State Gazette No. 38/10.05.2024, for the needs of the "Gene Expression Regulation" Section, with Dr. Kiril Todorov Kirilov as the sole candidate
Opinion prepared by Assoc. Prof. Dr. Anastas Gospodinov, Institute of Molecular Biology

I. Brief Biographical Information

Dr. Eng. Kiril Todorov Kirilov was born in 1974 in Sofia. He obtained his Master of Science in Engineering in Biotechnology from the University of Chemical Technology and Metallurgy (UCTM) in 2001. In 2014, he successfully defended his PhD thesis in Molecular Biology at the "Acad. Roumen Tsanev" Institute of Molecular Biology, Bulgarian Academy of Sciences (IMB-BAS), specialty code 4.3.
Dr. Kirilov's scientific career began at IMB-BAS, where he held the position of specialist until 2009, followed by research associate (third degree) from 2009 to 2011. Since 2011, he has been working as a Chief Assistant Professor in the "Gene Expression Regulation" Section.
He has undergone international research training, including at the International Centre for Genetic Engineering and Biotechnology in Trieste, Italy (2003, bioinformatics), and at Carleton University, Ottawa, Canada (2013). He is the author of 28 scientific publications with over 100 citations (Scopus h-index: 6), including 20 articles published in the last five years, several in Q1 and Q2 journals. He also holds two patents for educational kits in chemistry.
Dr. Kirilov is also actively engaged in teaching and student training. Between 2014 and 2021, he was a part-time lecturer in Bioinformatics at the Technical University of Sofia, delivering lectures and practical courses across several faculties, including "Computer Systems and Technologies," "English Engineering Education," "German Engineering Education and Industrial Management," and "Applied Mathematics and Informatics." From 2021 to 2024, he has taught at the New Bulgarian University (NBU), initially as an adjunct and later as Chief Assistant Professor in the Department of Natural Sciences, Bachelor Faculty. He has developed new courses in the field of biological sciences.

He has also made important contributions to the development and management of nationally funded research projects in the fields of bioinformatics, structural biology, molecular dynamics, and modeling. His work involves modern computational approaches and programming (Java, Python, Perl, VB), as well as the use of parallel computing platforms (including Intel Xeon Phi).

II. Publication Activity and Compliance with National Minimum Requirements

Dr. Kirilov presents a substantial body of scientific work that fully meets—and significantly exceeds—the national minimum requirements for the academic position of Associate Professor. He has submitted 25 publications for the competition, of which 19

are indexed in international databases such as Scopus and Web of Science. Six of the publications are proposed for his habilitation thesis, including four in first-quartile (Q1) journals with impact factors up to 8.2. His total points across all criteria amount to 494 (with 320 required).
His scientific work is interdisciplinary, covering molecular biology, neuropharmacology, structural bioinformatics, genomics, systems biology, and cellular biochemistry. He is first or last author on three publications and a key co-author on many others, contributing to experimental design, data analysis, and interpretation. A total of 93 citations are reported in Scopus (excluding self-citations), attesting to the impact and international visibility of his research.

III. Research Activity and Contributions

Dr. Kirilov's diverse scientific contributions can be categorized as follows:

1. Application of Computational Bioinformatics Methods in Drug Development

He employs in silico techniques such as molecular modeling, docking analysis, quantum chemical calculations, and virtual screening to develop therapeutic molecules targeting complex diseases like Alzheimer's, Parkinson's, and COVID-19. For instance, hybrid peptide-norgalantamine derivatives with 100-fold lower toxicity than galantamine and enhanced acetylcholinesterase inhibition were designed, shown to bind both the catalytic and peripheral sites of the enzyme.
He also contributed to developing neurotensin(8–13) analogues targeting NTS1 and NTS2 receptors, with improved blood-brain barrier permeability. The best-performing compound improved motor function and memory and protected dopaminergic neurons in a mouse model of Parkinson's disease.
A comparative study of the antiviral agents favipiravir and deferiprone revealed higher ACE2 and Mpro binding affinity and lower neurotoxicity for the latter. Advanced methods including SCXRD, HYDE, and DFT were used.
He also co-authored a bibliometric analysis of lycopene in nutraceuticals, focusing on its relevance to prostate cancer, cardiovascular diseases, and obesity.

2. Codon Usage and Context Analysis in Prokaryotic and Mitochondrial Genomes

Dr. Kirilov developed the software Gene Triplet Analysis (GTA) for codon frequency and context analysis in prokaryotic and mitochondrial genomes, using GenBank files. The tool enables analysis of both coding and regulatory regions.
He analyzed 158 prokaryotic genomes, classifying genes by expression level and showing taxonomic differences in codon usage. A correlation analysis revealed discrepancies between formal taxonomy and codon usage patterns. He also analyzed all 3904 codon pairs in *E. coli*, demonstrating a significant impact of 3'-terminal codon pairs on protein production.

3. Automated DNA Fiber Analysis Tool

He developed the Java-based DNA Size Finder, a lightweight tool for automated analysis of DNA fibers labeled with halogenated nucleotides. It employs Otsu segmentation,

modified Zhang–Suen skeletonization, and curvature control for precise length measurement. The software supports automated and manual modes, user profiles, and is cross-platform. Its results are comparable to manual analysis. The tool is open-source and available on GitHub.

4. Deglycation Activity of E. coli Phosphoglucose Isomerase

A novel deglycation function of the glycolytic enzyme Pgi was discovered—acting on Amadori products modified with glucose-6-phosphate. Pgi-proficient cells accumulated fewer glycated proteins than Pgi-deficient ones, even at lower G6P levels. Structural similarities with FrlB suggest an evolutionarily conserved secondary function.

5. Studies on Glycation and Related Biochemical Processes in E. coli and In Vitro

He investigated the inhibitory effect of six purine compounds on BSA glycation, showing theophylline and xanthine as strong inhibitors, while uric acid promoted glycation. L-lysine was shown to promote advanced glycation end-product (AGE) formation and protein aggregation even in the presence of antioxidants. *E. coli* was used as a model for AGE-related aging via chromosomal DNA damage.

6. Segregational Stability of Human IFNγ Plasmids in E. coli

He studied the effect of 3'-terminal variations in the human interferon-gamma gene on plasmid stability in *E. coli*. A plasmid with a 9-nt deletion was rapidly lost within 50 hours. A linear relationship was found between mRNA levels and plasmid loss rate. A mathematical model was applied to quantify instability parameters.

7. Conceptual Model for Breast Cancer Diagnosis and Precision Therapy

He developed an in silico model integrating medical imaging, histopathological data, molecular markers, and clinical data using AI algorithms (LYNA), machine learning (SVM, ANN, PCA), CAD diagnostics, and NGS profiling. Platforms like KNIME and Weka enabled automated processing for personalized diagnosis and treatment recommendations.

8. Educational Kits for Chemistry and Environmental Education

He developed two patented educational kits (BG2017/2560 and BG2017/3798) for high school students (grades 8–11), including reagents, glassware, and manuals with basic and advanced experiments. The aim is to increase interest in natural sciences and sustainable development through hands-on learning.

IV. Participation in Research Projects and Additional Academic Activity

Dr. Kirilov has participated in ten research projects, leading three of them, including one funded by the Bulgarian National Science Fund. He has contributed to infrastructure development, digital tools, and applied bioinformatics solutions. He also trains students and young researchers, including supervising graduate theses.

Conclusion

The submitted materials and analysis of Dr. Kiril Kirilov's scientific output demonstrate an interdisciplinary approach, high scientific level, and strong innovation. His work is characterized by significant practical applicability, aligning well with national and European scientific priorities. Based on the documents provided, Dr. Kirilov fully meets and significantly exceeds the requirements for the academic position of Associate Professor.
His extensive experience with cutting-edge bioinformatics methods offers excellent prospects for his academic development and that of the researchers that will work with him at IMB. I am confident that Dr. Kirilov will continue to play a leading role in advancing computational approaches in biology at our institute.

Therefore, I strongly recommend that the esteemed Scientific Jury vote in favor of electing Dr. Kiril Kirilov to the position of Associate Professor in the professional field 4.3. Biological Sciences, specialty Molecular Biology.

SIGNATURE: