

REVIEWER REPORT

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On the evaluation of the candidates in a competition for the Associate Professor's position at the Institute of Mineralogy and Crystallography - Bulgarian Academy of Sciences (IMC-BAS), announced in the State Gazette number 95/14.11.2023.

By virtue of Order No. 40RD09/22.01.2024 issued by the Director of IMC-BAS, I have been designated as a member of the scientific committee for the selection process pertaining to the academic position of Associate Professor within the area of higher education of Natural Sciences, Mathematics, and Informatics, with a specialization in Professional Direction 4.3: Biological Sciences (focusing on Crystallization and Structural Analysis of Macromolecules), meeting the requirements of the "Structural Crystallography and Materials Science" department.

I hereby affirm that I do not possess any conflicts of interest as defined under § 1, item 2a, nor am I subject to any restrictions concerning related individuals as outlined in § 1, item 5 of the supplementary provisions of the Law on the Development of Academic Staff in the Republic of Bulgaria (ZRASRB). Furthermore, I acknowledge having co-authored a conference abstract, identified as publication 16 under indicator "D", which I will abstain from evaluating. It's important to note that upon review, no instances of plagiarism were detected.

I. Submitted materials for the competition

One candidate submitted documents to participate in the announced competition - Dr. Hristina Ilieva Dimitrova, Senior Research Associate at the same institute. All the documents required by the ZRASRB, the Regulations for its application, and the Regulations on the terms and conditions for acquiring scientific degrees and for holding academic positions at the BAS, and IMC-BAS were provided to me in electronic form. The candidate has submitted a medical note, a criminal record certificate, and an official note from IMC-BAS, certifying work experience in the specialty of 4 years, 9 months, and 4 days, which makes her legitimate to participate in the announced competition.

II. Professional and academic development

In 2005, Dr. Dimitrova achieved a Master's degree from the Faculty of Biology at St. Kliment Ohridski University in Sofia, specializing in "Ecology and Environmental Protection" (Diploma No. 180056). Since 2011, she has pursued her doctoral studies at IMC-BAS. From 2015 to 2024, she has progressively advanced through various roles within the same institute, serving as an assistant (2015-2018), researcher (2018-2019), and currently as Senior Research Associate (2019-present). Throughout her tenure, she has been actively engaged in experimental work pertaining to structural and crystallographic analyses. Her expertise extends to mastering diverse diffraction methods and techniques essential for crystal growth, encompassing minerals, small molecules with biological functionalities, porous structures, and biological macromolecules.

During this period, Dr. Dimitrova successfully defended her doctoral thesis, earning the designation of Doctor in Mineralogy and Crystallography. Her research was focused on the topic "Crystallization and Structural Analysis of Two Palindromic DNA Sequences with Fluorescent Markers".

III. Scientific indicators

For participation in the competition, Dr. Dimitrova submitted a list of 23 publications. In the documents sent to me for the occupation of the academic position "Associate Professor" to the publications for obtaining the Ph.D. (2. Points achieved for holding the Ph.D., Indicator "D") an additional article/abstract that does not appear in NACID was added, as well as the indicated points, do not correspond to those published in the database. Since the list of 23 publications does not include her assets for the acquisition of a Ph.D., the noted facts will not be considered and impact my assessment.

From the publications presented in the "List of publications" of Dr. Hristina Ilieva Dimitrova I do not accept and do not evaluate the numbers:

10: "Business card of Dr. Hristina Dimitrova"; "Bulgarian Science" magazine (2021), December issue, pp. 18-21.; ISSN (WEB) 1314-1031. The article features Dr. Dimitrova and her involvement in the PERIMED Center of Competence. **Reason:** It is not a scientific publication with author Dr. Dimitrova.

12. Chayrov, R., Tencheva, Al., Sbirikova-Dimitrova, Hr., Shivachev, B., Kujumdzieva, A., Nedeva, Tr., Stankova, Iv..Synthesis, Antibacterial, and Antifungal Activities of Hybrid Molecules

Based on Alzheimer Disease Drugs and Bearing an Amino Acid Fragment. Proceedings, 41, 23, MDPI, 2019, ISSN:2504-3900, DOI:10.3390/ecsoc-23-06602, 1-11 (2019). **Reason:** The Proceedings publication has no SJR and Impact Factor (IF). Not scored for 4.3. Biological Sciences.

19. Hristov, P., Neov, B., Sbirikova, H., Radoslavov, G., Shivachev, B.. "Genetic polymorphism of kappa casein and casein micelle size in the Bulgarian Rhodopean cattle breed. Biotechnology in Animal Husbandry, 30, 4, Institute for Animal Husbandry, Belgrade-Zemun, 2014, ISSN:1450-9156, DOI:10.2298/BAH1404561H, 561-570. (2014). **Reason:** The publication Biotechnology in Animal Husbandry does not have SJR and IF. Not scored for 4.3. Biological Sciences.

Listed as papers numbered 15, 16, and 17 are published in Acta Crystallographica Section A-Foundations and Advances. I do not accept these conference abstracts as publications because they do not fulfill the conditions of item 14, "Additional provisions" of the ZRASRB, in the definition of a publication as a published scientific work. Evidence that "publications" 15, 16, and 17 are abstracts is evident from the journal's website <https://journals.iucr.org/a/issues/2018/a2/00/>. I evaluate the scientometric indicators based on 17 publications with information taken from the Thomson Reuters Web of Science and Scimago Journal & Country Rank databases.

Dr. Dimitrova has divided the presented list of publications into 2 parts and has clearly distinguished the articles that meet the criteria for holding the Associate Professor academic position according to the national minimum requirements (NMR). Under indicator "B," I have thoroughly evaluated all publications, awarding a total of 105 points. Notably, one of these papers was published in Q1, with the remaining four falling within Q2. However, it's important to note that under indicator "D," I do not consider the aforementioned abstracts, designated as publications numbered 10, 11, and 12. The breakdown of accepted publications by quartiles is as follows: 3 articles in Q1, 1 article in Q2, 2 articles in Q3, and 6 articles in Q4. Additionally, 3 articles - numbered 5, 7, and 14 - are not scored for Professional Direction 4.3, Biological Sciences, as previously mentioned. Hence, the total score for indicator "D" amounts to 197 points.

In this context, the candidate has provided a list of 85 citations for indicator "G". In accordance with the Regulations for the Application of the ZRASRB and the Regulations of the BAS and IMC-BAS, I approve a score of 170 points (refer to Table 1).

Table 1. Candidate's group indicators (A to D) following ZRASRB and the Regulations of BAS and IMC – BAS

Indicator's group	Indicators number	Minimum number of points	Candidate's points
A	#1 – PhD Degree	50	50
B	#4 – publications	100	105
G	#7 – publications	200 (220 for BAS)	197
D	#11 – citations	50 (60 for BAS)	170
Total		400 (430 for BAS)	522

Dr. Dimitrova's scientometric indicators **do not fully meet** the national minimum requirements for the academic position "Associate Professor". The group of indicators, according to Table 1 of the Regulations for the implementation of the ZRASRB (amended and supplemented by State Gazette No. 76 of September 5, 2023), are as follows: A1 (Ph.D. Thesis) – 50 points (required 50 points); B4 (habilitation thesis - scientific publications in publications...) - 105 points (required 100 points); D (publications) – 197 points (NMR 200, minimum 220 points (for BAS)) and D (citations) – 170 points (minimum 60 points). Despite the shortfall in indicator "D" with a required minimum of 430 points (for BAS), Dr. Dimitrova collects 522 points in the individual indicators.

Recommendation: Since, according to indicator B4 (scientific publications equivalent to a habilitation thesis), the candidate's points are not enough to cover the NMR, I recommend that she include additional publications that meet the conditions of the ZRASRB, which Dr. Dimitrova has available, evident from Scopus.

IV. Skills and aptitude for leading scientific research

Dr. Hristina Dimitrova has participated actively in developing scientific projects, having already led one. Their detailed distribution is shown in Table 2. Although they do not fall under the requirements for gaining points for the academic position of Associate Professor, the new academic position is expected to fully take over the management of their research both thematically and financially.

Table 2

Indicator	Number	Candidate's points
No. 14: Participation in a national scientific or educational project	2	20
№15. No. 14: Participation in an international scientific or educational project	1	20

№16. Leading a national scientific or educational project	1	20
№18. Funds raised for projects managed by the applicant	30 000 лв.	6

V. Scientific research activity

Dr. Dimitrova's research lacks systematic categorization into distinct directions. From my evaluation of the scientific works in which Dr. Dimitrova has participated in the competition (as presented in the List of Publications of Dr. Hristina Ilieva Dimitrova), it appears that **two primary research directions** emerge.

The first direction, encompassing the majority of publications (13 in total), focuses on investigations concerning the crystallization and structural elucidation of synthetic compounds such as oxonium 2,4,8,10-tetra-hydroxy-1,3,5,7,9,11-hexaoxa-2,4,6,8,10-penta-borasp[5.5]undecan-6-uide hydrate (20), Cinnamoyl-memantine hybrids (7), 2-Methylcinnamic Acid Amide in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (6), N,N-Dimethylglycine-Amantadine (5), Aminoadamantane (11), (1, 3), 5'-Oxosp[iro]-(fluorene-9,4'-imidazolidine)-2'-thione (8), fluorescent dyes (stilbazolium dyes, 18), as well as co-crystallization of drugs Aciclovir, Caffeine, Nitrofurazone, Theophylline, and Proline with 4-Halophenylboronic Acid (2), and copper complexes of Bis(1',3'-Hydroxymethyl)-Spiro-(Fluorene-9,4'-Imidazolidine)-2',5'-Dione (9), as well as investigation of modified urea and thiourea with tetraalkyl ammonium hydrogen sulphate (21).

The crystal structures detailed in the aforementioned papers have been acquired, analyzed, and subsequently deposited in the Cambridge Crystallographic Data Center, showcasing Dr. Dimitrova's adept and proficient growth in her field. This reveals her competent and professional development combined with an upgrade of her university major in Ecology with specific competencies in crystallography and structural analyses.

Note: In the "Author's Reference", contributions under the first direction are not clearly highlighted. In my opinion, **three important original scientific conclusions** stand out in the first direction of Dr. Dimitrova's research.

It has been shown that:

1. Newly synthesized and structurally characterized squaramides and squaramates show inhibitory activity against deoxyribonuclease I (DNase I) and xanthine oxidase in vitro. Three of these compounds are among the most potent small organic DNase I inhibitors tested to date. Interest in

DNase I inhibitors is high due to their essential role in various biological processes and pathologies (chronic obstructive pulmonary, neurodegenerative, cardiovascular, and autoimmune diseases).

2. Formation of co-crystals of 4-chlorophenyl boronic acid with various drugs (such as nitrofurazone, acyclovir, and theophylline) can change their biological activity and medicinal effect.

3. A new polymorphic structure of bisacodyl may change the understanding of its side effects.

Dr. Dimitrova's second research direction encompasses structural biology, focusing on the examination of various proteins and palindromic DNA sequences. These investigations are particularly significant as they are closely linked to numerous medicinal formulations and biologically active substances (2, 4, 13, 14, 22, 23).

Original scientific conclusion:

1. The crystal structure of DNA sequence 5'-GCCACACGGC-3' was obtained and characterized for the first time.

2. A new Thioflavin-T homolog has been synthesized and proven.

3. The structures of the tetradecamer DNA sequences d(CCGGGGTACCCCGG)₂ and d(CGTGAATTCACG)₂ were characterized.

4. The interaction of Lysozyme with nano-sized TiO₂ particles has been proven.

5. The crystal structure of co-crystallization forms of the DNA sequences 5'-CGTGAATTCACG-3' and 5'-CGCGAATTCGCG-3' with the fluorescent markers DAPI, Berenil, AK3-4, AK3-9, DL72, DL89, and EtBr was studied.

6. Six original structures (5T4W, 5JU4, 5NT5, 6G5C, 8ASK, 8ASH) have been deposited in the PDB database.

I designate the development of a rapid and straightforward methodology for preparing biological samples, specifically bacteria and DNA, for observation using a scanning electron microscope (23) as a **significant applied-scientific contribution**.

VI. CONCLUSION

Dr. Dimitrova's application does not fully meet the requirements of the ZRASRB, its rules for application and the regulations of IMC-BAS and BAS for holding the academic position "Associate Professor". Nevertheless, she has made significant scientific and applied-scientific

contributions, evidenced by her publication records in prestigious scientific journals and their citation. Dr. Dimitrova has a clearly defined scientific research profile in structural biology and methodological training in crystallization and structural analysis of macromolecules. All this gives me a reason to recommend to the respected members of the Scientific Council of IMC-BAS to give their positive vote for the election of assistant professor Hristina Dimitrova, Ph.D., to the academic position "Associate Professor" after implementing my recommendation.

22.03.2024

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