OPINION

on a competition for the academic position **"Professor"** in professional direction **4.3. Biological Sciences**, scientific specialty **"Immunology"**, announced for the needs of the Department of Immunology, Laboratory of Experimental Immunotherapy at the Stefan Angelov Institute of Microbiology at the Bulgarian Academy of Sciences in SG No. 84/10.10.2025 with a **single candidate, Assoc. Prof. Dr. Anastas Dimitrow Pashov** from IMicBio – BAS

The opinion was prepared by ***Prof. Nevena Ilieva-Litova, PhD*** (IICT – BAS), member of the scientific jury for the competition, according to Order № I-170 от 28.10.2025 of the Director of the IMicBio – BAS

1. Brief Biographical Data of the Candidate

The sole candidate in the present procedure, Assoc. Prof. Anastas Dimitrov Pashov, MD, PhD, graduated from the Medical University of Sofia (then the Medical Academy) in 1989. Immediately after graduation, he commenced doctoral studies (then referred to as aspirantura) at the National Center of Infectious and Parasitic Diseases, Sofia. In 1995, he successfully defended his PhD thesis entitled *"Identification and Quantitative Characterization of the Expression of Two Pan-Leukocyte Antigens Recognized by Newly Generated Monoclonal Antibodies CAF7 and 7E12."* Since 1993, he has also practiced as a physician at the same institution.

His academic career began in 1998 at the Institute of Biology and Immunology of Reproduction, Bulgarian Academy of Sciences (BAS), where he obtained habilitation in 2000 (Senior Researcher, II degree). Following postdoctoral fellowships totaling nearly ten years at a specialized research unit of Pierre and Marie Curie University (INSERM U430) and at the University of Arkansas for Medical Sciences (USA), he won a competition for the position of Associate Professor in 2010 at the Institute of Microbiology, Bulgarian Academy of Sciences, where he has been employed to date. Since 2015, he has served as Head of the Laboratory of Experimental Immunotherapy.

The candidate has substantial experience in the implementation and leadership of research projects. He has participated in four and led two nationally funded projects; participated in two and served as Principal Investigator in two internationally funded or EU Framework Programme projects (one of which was a Marie Curie Reintegration Grant), attracting significant external funding to the institute through these initiatives.

Assoc. Prof. A. Pashov has supervised and co-supervised two successfully defended PhD students and three graduate (Master's) students. During the periods 1997–2001 and 2014–2015, he delivered courses in Tumor Immunology.

2. General Description of the Submitted Materials

For participation in the competition, the candidate has submitted a complete set of documents required under the Law on the Development of the Academic Staff in the Republic of Bulgaria and the specific requirements of the respective procedure in accordance with the Regulations for the Acquisition of Academic Degrees and the Occupation of Academic Positions at the Institute of Microbiology, Bulgarian Academy of Sciences (IMicBio – BAS). The competition materials are organized in a somewhat unconventional manner. I accept the assessment of the committee at IMicBio – BAS regarding their compliance with the institutional regulatory requirements.

Assoc. Prof. Anastas Pashov's total impact factor amounts to 283; his publications have been cited nearly 1,500 times, and his Hirsch index is 20. For this competition, the candidate has submitted 51 publications that have not been used in previous procedures. Of these, 35 replace the habilitation thesis for the academic position of "Professor" (Group B indicators), while the remaining 16 meet the requirements under Group G indicators. In 17 of these publications, the candidate is first or corresponding author, underscoring his substantial contribution to the reported results. The findings of these studies have been presented in 24 communications at 7 national and 13 international scientific forums. The publications are grouped according to the quartiles of the respective journals, which is not particularly constructive. Lists with unified numbering of all publications and, separately, of those submitted for the present competition would have provided greater clarity and facilitated the analysis.

3. General Characterization of the Scientific Activity and Main Scientific and Applied Contributions of the Candidate

The candidate's scientific research encompasses a broad and interdisciplinary spectrum situated at the interface between molecular immunology, antibody biophysics, and contemporary bioinformatic approaches for immune repertoire analysis. A central theme of his research is the re-evaluation of the concept of antibody specificity and the role of polyreactivity and idiotypic connectivity as fundamental, evolutionarily conserved characteristics of the immune system.

I will focus in greater detail on *the results in the field of bioinformatic technologies and systems immunology*. The most original and conceptually significant contributions of the candidate are related to the *development and application of bioinformatic and systems biology approaches* for the analysis of the antibody repertoire at the level of functional specificity (the Igome). The candidate is among the pioneers in the development of *Igome analysis methodology*, in which, instead of sequencing B-cell receptors, libraries of mimotopes, peptide microarrays, and high-throughput binding assays are employed. This approach enables direct mapping of the space of antibody specificities and overcomes a fundamental limitation of AIRR-seq methods, namely their lack of information on antigen specificity.

A comprehensive *bioinformatic pipeline* has been developed, comprising:

- selection and reduction of mimotope libraries;
- definition of isospecificity using ROC-optimized metrics;
- construction and analysis of *Igome graphs* and *cross-reactivity networks*;
- machine learning methods for the extraction of diagnostic signatures.

These methods have been successfully applied to the identification of repertoire biomarkers in a number of complex diseases. Particularly impressive are the results obtained in:

- **glioblastoma**, where a compact set of IgM reactivities was defined that discriminates tumor patients from controls and from patients with brain metastases;
- **neurodegenerative diseases** (Alzheimer's disease and frontotemporal dementia), in which a systemic disruption of the public IgM repertoire and idiotypic connectivity was demonstrated, accompanied by the emergence of restricted but highly represented IgG clusters;
- **antiphospholipid syndrome**, which is characterized not only by the appearance of pathogenic IgG, but also by the loss of entire classes of natural IgM reactivities.

A particularly important scientific contribution is the demonstration that the *loss of repertoire diversity*, and not solely the emergence of new autoreactivities, constitutes a key hallmark of immune dysregulation. This represents a substantial extension of classical concepts in autoimmunity.

The bioinformatic analyses are complemented by interpretable models that enable linking repertoire alterations to idiotypic theory and the individual's immunological history. The scripts and

algorithms developed by the candidate are publicly available and provide a sustainable foundation for future research.

4. Scientometric Indicators

The presented scientometric data (publications, independent citations, and effective evaluation of project and teaching activities) ***substantially exceed the requirements set forth in the Law on the Development of the Academic Staff in the Republic of Bulgaria and its Implementing Regulations, as well as the specific requirements of the Bulgarian Academy of Sciences and the Stefan Angelov Institute of Microbiology***. For the academic position of "Professor," a total of 640 points across all indicators is required; the candidate participates in the present competition with a total of 4,508 points, i.e., seven times above the minimum requirements.

5. Critical remarks

I have no critical remarks that would affect my overall assessment.

6. Personal Impressions of the Candidate

I have known Assoc. Prof. Anastas Pashov for nearly ten years through our collaboration on multidisciplinary projects encompassing both laboratory and in silico studies of immunoactive biomolecules, mechanisms of action of viral proteins, and approaches for their inactivation. I have also attended his presentations at seminars and scientific forums. Over the years, my opinion of him has been firmly established as that of an exceptionally erudite researcher with creative thinking, original ideas, and broad expertise enabling their effective realization. I consider this new phase in his professional development – the professorship – to be significantly overdue, and I am convinced that he is well prepared to meet many further creative challenges.

7. Conclusion

Taken as a whole, the candidate's scientific achievements demonstrate a ***high degree of originality, methodological depth, and international visibility***. Of particular value is his contribution to the ***introduction of systems biology and bioinformatic thinking into immunology***, opening new perspectives for the diagnosis and understanding of complex immunopathological conditions. This clearly transcends the traditional boundaries of the discipline and is fully commensurate with the requirements for the academic position of "Professor."

I am convinced that Assoc. Prof. Dr. Anastas Pashov is fully deserving of appointment to the academic position of "Professor" in Professional Field 4.3. Biological Sciences, Scientific Specialty "Immunology," and I therefore propose that the Scientific Jury recommend to the esteemed Scientific Council a positive decision regarding his application in the announced competition for the needs of the Department of Immunology, Laboratory of Experimental Immunotherapy, at the Stefan Angelov Institute of Microbiology, Bulgarian Academy of Sciences.

12 February 2026   signature:

/Prof. Nevena Ilieva, PhD/