O P P I N I O N

by Corresponding Member of BAS Svetozar Dimitrov Margenov,
Professor at IICT - BAS,
on materials submitted for competition
to take the academic position "Associate Professor" at IICT - BAS
in professional field 4.5 Mathematics, scientific specialty
"Mathematical Modeling and Application of Mathematics (Applications in
Computational Physics and Biology)"

In accordance with Order № 21/15.03.2022 of the Director of IICT – BAS, I have been approved as a member of the scientific jury under the competition for Associate Professor, announced in the State Gazette (issue 21 of 14.03.2022). Documents for participation in the competition are submitted by Dr. Elena Boyanova Lilkova, Senior Assistant Professor at IICT - BAS.

1. Brief biographical information

Senior Assistant Professor Elena Boyanova Lilkova has graduated in 2009 from the Faculty of Physics at Sofia University "St. Kliment Ohridski" holding a Master's Degree in Medical Physics.

In the period 2011 г. – 2015 г. she has been a post-graduate student at the same university, where she has defended her dissertation for the educational and scientific degree "doctor" (PhD) on the topic "Investigation of human interferon gamma employing molecular dynamics simulations". Since March 2015, she has been working at IICT, successively holding the positions of programmer and Assistant Professor. In December 2017, she was elected Senior Assistant Professor, in which position she still works in Section "Scientific Computations with Laboratory for 3D Digitization and Microstructure Analysis".

2. General description of the materials presented

The materials presented by Senior Assistant Professor Elena Lilkova are prepared in accordance with the Development of Academic Staff in the Republic of Bulgaria Act (DASRBA), the Regulations for the Application of DASRBA (RADASRBA), as well as with the specific requirements of the Regulations of BAS and IICT - BAS. They include: European CV; copy of Diploma for the educational and scientific degree "Doctor"; certificate of work experience; list of scientific publications; list of scientific publications for participation in the competition; abstracts of scientific publications for

participation in the competition – in Bulgarian and English; copies of scientific publications for participation in the competition; reference for fulfillment of the minimum requirements of IICT; reference for fulfillment of the minimum requirements of National Center for Information and Documentation (NCID); reference to original scientific and applied scientific contributions; statement that there is no proven plagiarism. Also presented are electronic media with information, according to the requirement of IICT.

For participation in the competition, Senior Assistant Professor Elena Lilkova has presented 21 scientific publications covering the period 2010 – 2021 (12 of them are published during last 5 years). Of these, 14 are indexed in Scopus and/or WoS. All publications are in English. There are 4 papers in specialized scientific journals with Impact Factor (IF), 2 of which are in Quartile Q1 (International Journal of Molecular Sciences). 13 of the other articles are in specialized series with SJR. Out of the submitted publications, 5 are with 4 co-authors, 3 - with 5, 6 - with 6, and 7 with more than 6 co-authors. The points for each of the indicators meet the requirements, and for indicators D and E they significantly exceed them.

3. General characteristics of the applicant's activities

Senior Assistant Professor Elena Lilkova is an established scientist in the field of mathematical modeling and the application of mathematics in computational physics and biology. Mathematical modeling and computer (including supercomputer) simulations are the basis of the research methodology in the presented works. Specialized approaches for validation and software tools for visualization of the obtained results have an important place in this type of research.

In the documents of Senior Assistant Professor Lilkova is documented participation in 10 national scientific projects, 9 of which are under contracts with the Bulgarian Science Fund. She has managed two projects under the Young Scientists Support Program.

In recent years, she has been a member of organization or program committees of the following international scientific forums: Large Scale Scientific Computations (LSSC'17, LSSC'19, LSSC'21); Numerical Methods for Scientific Computing and Advanced Applications (NMSCAA'18); Annual Meeting of Bulgarian Section of SIAM (BGSIAM'18, BGSIAM'19, BGSIAM'20, BGSIAM'21).

Senior Assistant Professor Elena Lilkova is co-editor of 4 volumes in series of Springer with SJR, containing papers on talks from the BGSIAM'18 - BGSIAM'21 conferences.

4. Scientific and applied scientific contributions

The presented scientific and applied scientific contributions of Senior Assistant Professor Lilkova are in accordance with the scientific specialty "Mathematical Modeling and Application of Mathematics (Applications in Computational Physics and Biology)".

Molecular dynamics is one of the most effective approaches for modeling multi-particle atomic and molecular systems. The processes are described by a highly nonlinear Schrödinger equation, for the numerical solution of which state-of-the-art numerical methods, algorithms and software tools are applied. This is a basic apparatus used by the candidate. The results of Senior Assistant Professor Lilkova also include specialized numerical methods for: calculation of free energy; accelerated traversal of the phase space; protein folding, predicting the binding of proteins to ligands or other proteins and macromolecules.

The results of Senor Assistant Professor Lilkova have a complex interdisciplinary character. It is important to note that the analysis of protein structure and dynamics is a complex process with a number of open problems. The basis of the presented results is the synergy of complementary approaches in which the numerical solution of deterministic non-stationary partial differential equations and topological techniques are combined.

I accept the applicant's proposed classification of the main results presented in the following three groups:

I. Molecular modeling of human interferon gamma;
II. Modeling of antimicrobial peptides;
III. Scientific software.

I.   Molecular modeling of human interferon gamma

Human interferon gamma is known to be a very important signaling molecule (cytokine) that plays a key role in producing and modulating the body's immune response. This is a major reason for studying its structure, dynamics and interactions with other biological molecules.

It is noted that the results presented in this section may be used by scientists at the Institute of Structural Biology in Grenoble, France, to develop potential biological agents to inhibit endogenous interferon gamma. This group of results is published in works [B1, B2, B3, B4, D1, D4, D9, D10, D11].

The role of structure modeling in the search for answers to questions related to the impact of the last amino acids located at the C-terminal part on biological activity is explained. As an important achievement, I would like to point out the complete model of the structure of human interferon gamma obtained for the first time. This structure is used in subsequent works. Also included in this group of results are studies of:

mutant forms of human interferon gamma; impact of glycosylation on stability and structure; interaction with glycosaminoglycans.

II.   Modeling of antimicrobial peptides

Computer simulations (scientific computations) are established as a third independent branch of science, complementing traditional theoretical and experimental research. In particular, *in silico* experiments significantly shorten the time in all types of biomolecular research and in particular in the drug development process. The possibility of the results presented in this section being used by scientists from the Institute of Molecular Biology of the BAS has been noted. This group includes papers [D5 – D8, D12].

For example, in article [D5], the structure of the antimicrobial peptide magainin 2 (MG2) was analyzed, as well as that of its analogue with two point mutations MG2m. The results show that the two peptides have significantly different free energy profiles. The MG2 profile is shallow and rich in local minima, while that of the MG2m counterpart is much flatter, with only two well-defined minima. In work [G8], the secondary structure of peptides isolated from the antimicrobial mucus of garden snails was investigated. The obtained information on the secondary structure of the isolated new glycine-rich peptides enables an even deeper analysis of their functions and interactions. This group of results also includes studies of behavior and self-organization in solution and interaction with membranes.

III.   Scientific software

Numerical and computer modeling of biological objects forms a class of tasks with large computational complexity (Large Scale Problems). Solving them requires the development, optimization, maintenance and development of specialized high-performance computing (HPC) software. The presented results in this direction have a significant role in determining the complex contributions of Senior Assistant Professor Elena Lilkova within the framework of the current procedure. They can be defined as scientific and applied. They were published in works [D3, D13 – D17].

In papers [D3, D13] the parallel performance (parallel scalability) of the specialized software packages GEANT4, GROMACS and NAMD was analyzed. The studies have experimental nature, and for this purpose numerical tests were conducted on state-of-the-art supercomputer architectures. For example, the Avitohol supercomputer has hybrid Intel Xeon architecture with Intel Xeon Phi co-processors. It is shown that the highest performance is achieved when adaptive time stepping is used. An important issue is achieving synergy (balance) between performance and sustainability.

Papers [D14 – D16] present the results of the developed specialized approaches and software tools for molecular modeling of biological systems. The aim is to improve the computational efficiency in accounting for non-local electromagnetic interactions

using an external parallel computing library. I would also note the improvement of the convergence of the iterative method based on the combined use of the conjugate gradient (CG) method and the stabilized bi-conjugate gradient (BiCGSTAB).

In conclusion, I will note that the presented scientific and scientific-applied contributions are result of complex competences in several scientific fields, which include computational mathematics, physics and biology, as well as parallel programming and supercomputing applications.

5. Impact of the applicant's scientific publications

The list submitted by the candidate includes 26 independent citations. All of them are in publications that are indexed in Web of Science and/or Scopus. According to Scopus, the h-index of Senior Assistant Professor Lilkova is equal to 3. In the framework of the present procedure, the citations are presented in a separate table of data related to the group of indicators E. When 70 points are required, the evaluation of the listed citations is 156 points. All citations in the table are in works of foreign authors, including those published in a number of the most highly ranked specialized international journals and series.

6. Evaluation of the applicant's personal contribution

I accept as a general assessment, that in the joint works, Senior Assistant Professor Elena Lilkova has an equal role.

7. Critical remarks

I don't have any substantial critical remarks about the materials of Senior Assistance Professor Elena Lilkova, presented for the competition. They fully comply with the requirements of the DASRBA, RADASRBA, the regulations of BAS and the specific requirements of IICT – BAS.

The list of scientific publications includes 5 PRACE Whitepapers. In the table of data by group of indicators D, they are correctly reflected with 0 points each. Reviewing the results presented in them gives me reason to believe that it would be good if they (or at least some of them) were published in publications with better visibility from researchers working in this interesting area of supercomputing applications.

8. Personal impressions

I have known Elena Lilkova since 2008, as a member of the scientific team of the Center for Excellence "Supercomputing Applications" project, funded by the Bulgarian NSF, of which I was the coordinator. She was very actively and

successfully involved in the work on WP10: Supercomputer simulations of biological molecules and systems. The successful collaboration was the basis of her transition to the Scientific Computing Department of IICT - BAS in 2015.

I highly appreciate the scientific and professional level of the candidate, which determine Senior Assistant Professor Elena Lilkova as a qualified, correct and responsible scientist and colleague with proven abilities to work in a team. The active position on issues related to the joint work, as well as the responsiveness and willingness to help are an important part of the qualities that colleagues in the section highly value.

9. Conclusion

After getting acquainted with the materials on the competition, the complex evaluation of the applicant's qualities, including the scientific and scientific applied contributions, **I strongly recommend Senior Assistant Professor Elena Boyanova Lilkova to be elected to the academic position of "Associate Professor" at IICT - BAS** in professional field 4.5 Mathematics, scientific specialty "Mathematical Modeling and Application of Mathematics (applications in Computational Physics and Biology)".

11.07.2022
Sofia

На основание
ЗЗЛД