Report

on the materials presented for participation in the competition for the academic post of *Associate Professor* at the Institute of Organic Chemistry with Center of Phytochemistry - Bulgarian Academy of Sciences (BAS) in *Natural sciences, mathematics and informatics*, professional field 4.2. *Chemical Sciences*

Reviewer: Prof. Ilza Konstantinova Pajeva, DSci, PhD
Institute of Biophysics and Biomedical Engineering – Bulgarian Academy of Sciences

The only candidate in the competition for "Associate Professor" announced in the *State Gazette*, issue 43/31 May 2019 and on the website of the Institute of Organic Chemistry with Center of Phytochemistry (IOCCF) – BAS, is **Senior Assistant Dr. Miroslav Angelov Rangelov** from the same institute.

1. General presentation of the procedure and of the applicant

The materials presented by Dr. M. Rangelov are in accordance with the Regulations for the Development of the Academic Staff of IOCCF-BAS and meet the requirements of the Institute for the academic post "Associate Professor".

In the competition the candidate has presented 17 scientific publications (excluding those used in the PhD thesis), which are related to the subject of the competition and are accepted for review. Of these, 9 are published in journals of category Q1, 4 - of Q2 and 3 - of Q4. Indicator V lists 5 articles (3 of Q1, 2 of Q2) and indicator D - 11 articles (6 of Q1, 2 of Q2, 3 of Q4). In the list an Elsevier's book chapter is also included. Information is provided on: 52 citations; 46 participations in national and international scientific forums (3 of which are on the topic of the doctoral thesis); 23 national and international scientific projects (of which the indicator E includes: participation in 5 international projects, leadership of 1 national and of a team of 1 international scientific project). Funds of projects managed by the applicant are also presented. In terms of indicators V, D, G and E, the applicant exceeds the required number of points set by IOCCF-BAS.

Dr. Rangelov's biographical record shows that his higher education and his subsequent academic development are in the professional field of the competition. The applicant's professional experience is entirely related to his work at IOCCF, in which he has been awarded a PhD degree and has been working steadily since 2002. These facts suggest that Dr. Rangelov's research is related to the scientific topics of the Institute and suggests as well future benefits to the Institute's research staff from his habilitation.

2. General characteristics of the applicant's activities

***Contributions*.** Dr. Rangelov's main contributions relate to theoretical modeling studies of the ribosome functioning, and in particular to the catalytic mechanism of the peptide bond formation. The focus of research is the aminolysis reaction used as a model system to elucidate this mechanism. In general, these contributions relate to the development and implementation of a systematic approach to study aminolysis by selecting adequate methods and by a meaningful analysis of the obtained results as follows: finding the energetically most favorable reaction route; evaluation of the effect of the vicinal hydroxyl group (2′-OH) in different model systems; assessment of the hydrogen bonding capacity of different functional groups in respect to their potential interaction with the vicinal hydroxyl group. In these studies, the applicant has original elaborations implemented in the MolRan software package, incl. the highly informative and

illustrative catalytic maps for analyzing the effects of proton-donor or proton-acceptor groups according to their position relative to the reaction center. To perform successful modeling studies, Dr. Rangelov has constructed a complete ribosomal structure (of *E. coli*) based on available PDB structures and has proposed an approach to molecular dynamics simulations of the ribosome in a physiologically relevant environment by addition of metal ions to neutralize the charges of the phosphate groups in the RNA structure.

The "ribosomal" topic is presented by 9 articles, 4 of which are listed in section V and 5 – in section G. The Extended Habilitation Report does not refer to the publications of Bayryamov et al. in *JACS Communications* (2007) and *Protein and Peptide Letters* (2009).

Other contributions of the candidate relate to the application of the structure-based drug design method known as docking for studying various classes of biologically active compounds by means of the specialized module in MOE software package of CCG Ltd. Four publications (1 in V and 3 in G) on this topic are described in the Extended Habilitation Report under item 2 "*Other activities concerning revelation of ribosomal action and applying developed methodology on other systems*". In fact, these studies are not related to application of "*the developed methodology*" and represent a different and independent part in his contributions.

One of the presented papers relates to *in silico* modeling of single-chain variable fragment antibodies (scFv), by which the applicant contributes to the construction of a 3D homology model of the inhibitory antibody scFv A1 that is used to find conformational and electrostatic similarity to the native molecule C1q. The model is useful for understanding the recognition mechanism of the native molecule.

The last 3 publications relate to chemical analyzes of archaeological sites and exploration of the Black Sea. These works are not described in the Extended Habilitation Report.

The applicant's contributions can be classified as scientific and applied. The scientific contributions relate mainly to the modeling studies of the ribosomal catalytic mechanism. These contributions are described in the Extended Habilitation Report and include more than half of the publications used in the competition. The applicant's contributions related to docking and homology modeling of antibodies are of predominant scientific value, while those related to the research of archaeological sites and the Black Sea belong to the group of applied scientific contributions.

Scientific metrics. Dr. Rangelov has published his research results mostly in renowned scientific journals with high impact factor (IF), such as *ACS Communications* (IF = 7.885), *ACS Chemical Biology* (IF = 5.331), *Journal of Organic Chemistry* (IF = 4.002), *Food and Chemical Toxicology* (IF = 3.977), etc.. Actually, 16 out of 17 publications are in IF journals, of them 9 are in category Q1, what is an indicator for their quality. The list of citations includes 8 publications of the candidate, published in the period 2005-2011, which have been cited 52 times in the period 2008-2012. Dr. Rangelov has more citations, but the list provided by him for this competition gives enough points for indicator D. The Web of Science author search results in 22 publications, cited over 200 times and h-index of 9. The scientific metrics of the candidate certify international recognition of his results.

Assessment of the personal contribution. I evaluate the personal contribution of the candidate on the basis of his position in the list of authors, the results reported in the publications in accordance with his competence and the contributions described in the Extended Habilitation Report. In the publications on molecular aspects of the ribosomal catalytic mechanism, Dr. Rangelov is the 1st author in 4 publications, his main contributions being related to realization and interpretation of the quantum-chemical calculations. In 4 publications related to studies of

bioactive compounds that are interdisciplinary and combine wet lab and modeling investigations (docking), I estimate the candidate's contribution to modeling research. Considering that each of the three elements of such research (synthesis, testing and modeling) has its own significance for the end results, I recognize Dr. Rangelov's contribution as equivalent to that of the other authors. In the study on conformational changes in modeling of single-chain variable fragment antibodies, the candidate is the first author and has made a major contribution to the study. I cannot estimate the personal contribution of Dr. Rangelov in the publications on the chemical analyzes of archaeological sites and I suggest that they relate to the applicant's analytical and experimental skills. In "The Black Sea" chapter of Elsevier's book "World Seas: An Environmental Evaluation" there is a note that all authors except the 1st have an equal contribution, in this sense I regard the applicant's contribution again as equivalent to that of the other authors.

3. Critical comments and recommendations

I have a note on the formulation of item 2 in the Extended Habilitation Report related to the thematic differentiation of the candidates' contributions, which I mentioned above. The same report also mentions about "molecular dynamics simulation on all atom model of the whole *E. coli* ribosome was done and its model for drug design was prepared" (quoting number 13o for an abstract of 2014). Such a statement should be verified and I would recommend that the candidate do so in his future studies.

CONCLUSION

The documents and materials presented by Dr. Miroslav Rangelov meet the requirements of the Act for the Development of the Academic Staff in the Republic of Bulgaria (ADASRB), the Regulations for the Implementation of ADASRB, the Regulations for the Implementation of ADASRB of BAS and the specific Regulations of IOCCF-BAS.

The candidate has submitted a sufficient number of scientific papers published after the defense of his PhD thesis. According to the main indicators he collects points above the minimum required by the IOCCF criteria. In this way, the results achieved by Dr. Rangelov fully comply with the specific requirements of the IOCCF-BAS Regulations for the implementation of ADASRB.

Dr. Rangelov has original scientific and applied contributions, some of which have been published in renowned scientific journals with a high impact factor gaining in this way international recognition. In most publications he has a leading position and a distinguished personal contribution to the presented results, which defines him as a scientist with an individual academic profile.

The above gives me a reason to assess positively his candidature and to recommend to the Scientific Jury to prepare a report proposal to the Scientific Board of IOCCF-BAS for the election of **Dr. Miroslav Angelov Rangelov as Associate Professor** in the professional field 4.2. Chemical Sciences (scientific specialty "Bioorganic Chemistry, Chemistry of Natural and Physiologically Active Substances").

15.09. 2019 г. .....

Prof. Ilza Pajeva