

REPORT

on the materials presented by the candidate in a competition for the academic position of "Professor", 4. Natural Sciences, Mathematics and Informatics, 4.3 Biological Sciences, Biophysics, Electroinduced and Adhesive Properties Department, Institute of Biophysics and Biomedical Engineering, Bulgarian Academy of Sciences (IBPhBME-BAS),
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Reviewer: Prof. Dr Victoria Vitkova Vitkova, Georgi Nadjakov Institute of Solid State Physics, Bulgarian Academy of Sciences, a member of the Scientific Jury
according to order no. 541 / 29.09.2021

Candidate: Associate Professor Dr. Biliana Pancheva Nikolova-Lefterova, IBPhBME-BAS

General overview: Assoc. Prof. Dr. Biliana Pancheva Nikolova-Lefterova, the only candidate for the announced academic position, was appointed associate professor at the Institute of Biophysics and Biomedical Engineering, BAS in 2013. In compliance with the requirements of Article 29, Paragraph 1 of the Act for the Development of Academic Staff in the Republic of Bulgaria (ADASRB) in this competition Dr. Nikolova submits a list of 25 scientific papers covering the period from 2013 to 2021. Her scientific achievements regard electroinduced phenomena in cells and adhesive behaviours in the context of their application for developments of new diagnostic and electrochemotherapeutic strategies in biomedicine. The studies performed focus on the influence of established and novel antitumor agents on cell survival, the redox state and other parameters of cancer cell lines treated by electroassisted introduction of active substances into the cell.

The habilitation collection of papers corresponding to C group of indicators comprises 6 publications in referenced (Web of Science and Scopus) international journals, published in the period 2013-2021 and placed in the following quartiles, namely: Q1 - one publication; Q2 - four papers and Q3 - one contribution. The publications presented in addition to the habilitation work are 19. This number comprises 15 articles in referred international journals, 11 of which have been published in journals with impact factor referenced in JCR database. The publications in SJR and JCR referenced journals are distributed as follows: two publications in category Q1, five in Q2, four in Q3, and four papers in Q4. Four publications not referenced and indexed in the databases mentioned above are also presented. The articles comprising the activity in D group of indicators have been published in the period 2014-2021. The quantitative assessment exceeds the minimum number of points by groups of indicators C and D set in the Regulations for application of ADASRB. Assoc. Prof. Nikolova participates in the competition with 163 independent citations of her papers in scientific journals, referenced and indexed in the above databases. This citation record brings her 326 points, which exceeds almost three times the threshold required by indicator E in compliance with all requirements of the ADASRB, the Regulations for its implementation and the respective regulations for application of the act in BAS and the additional IBPhBME-BAS regulations.

General characteristics of the scientific, applied and pedagogical activity of the candidate: The main scientific results and achievements of the candidate are in the field of electroinduced phenomena and the adhesive behaviour of cells. They are included in 47 scientific publications and

are presented at 43 scientific forums, 28 of which are international congresses and conferences. Her scientific and administrative activities comprise the management of a research unit. She is the head of Electroinduced and Adhesive Properties Department at IBPhBME-BAS. Since 2019 Assoc. Prof. Nikolova has been a member of the Scientific Council of IBPhBME-BAS. She was a member of scientific juries for awarding the scientific and educational degree “Doctor”, as well as for the assessment of candidates for the academic positions “Assistant Professor” and “Professor” in procedures at ISSP-BAS, IBPhBME-BAS and Sofia University “St. Kliment Ohridski” (Faculties of Biology; Medicine; and Chemistry and Pharmacy) as well as at Medical University of Sofia (Faculty of Pharmacy).

The pedagogical activity is an important part of the Assoc. Prof. Nikolova’s record. She has been the supervisor of 3 successfully defended MSc theses. She has also supervised undergraduate students in the framework of EU Operational Programs “Human Resources Development” and “Science and education for smart growth”. Assoc. Prof. Nikolova is one of the supervisors of a successfully defended PhD thesis as well as the scientific consultant of 3 research projects lead by young scientists.

The management of two projects funded by Bulgarian National Science Fund and by the European Commission, as well as of two internal institutional projects evidences the fruitful scientific and organizational activity of the applicant. Assoc. Prof. Nikolova participates in the research teams of 9 international projects and of 8 projects with national funding. She is a reviewer of authoritative scientific publications of IOP, SPIE, MDPI, etc. Dr Nikolova is a guest editor of the MDPI Journal Separations (Q2).

Main scientific and/or applied contributions: The main candidate's achievements are in the field of electroassisted manipulation of cells and active substances, which finds biomedical application in tissue engineering, regenerative medicine, for electrotransfection and electrotransformation of cells, electrofusion, sterilization, vaccine elaboration and in the treatment of some genetic diseases and tumours. Reversible electroporation with a clinical focus is applied in electrochemotherapy for increasing the chemotherapeutics concentration in the neoplastic cells through targeting, internalization, and retention of nanoparticles in tumors. Elaboration of the existing and development of new combinations of electrochemotherapy and sustainable nanoscale drug delivery systems are promising for future therapeutic strategies in the personalized treatment of solid tumours.

Based on the research publications, in which Assoc. Prof. Nikolova is the first or corresponding co-author, the following main contributions stand out, related to new achievements in electroporation-based cancer treatment techniques in view of their potential in the field of drug vectorization, optimization of electrical parameters and the elucidation of molecular mechanisms of interaction. The application of polymersomes as carriers of contrast agents for lymph node mapping and for drug delivery in the treatment of metastases has been studied. Their effectiveness as a matrix for the development of nanoformulations with theranostic capabilities is evidenced. It has been found that even at low concentrations of heteropolysaccharides isolated from red microalgae, in combination with electrotherapy, a significant reduction in the survival of human lung adenocarcinoma cells is achieved. The effect of electrochemotherapy in the treatment of human skin neoplasms was studied by optical biopsy, namely analysis of the autofluorescence spectra of lesions and healthy tissue. Changes in morphology, adhesive properties, viability and migration in human

breast cancer cell lines induced after trehalose lipid treatment have been reported. Based on theoretical evaluations and molecular modeling, a mechanism of action is proposed involving membrane asymmetry between the outer and inner monolayers of the bilayer triggering the endosome formation. Sensitivity to treatment with rhamnolipid biosurfactants has been demonstrated for the same types of cancer cell lines. The observed effect is related to the process of autophagy, and a possible mechanism of membrane remodeling by endosome formation is shown. Significant contributions have also been made to revealing redox state and its relationship to the treatment of neoplastic disease. The effect of combinations of chemotherapeutic drugs on the growth of implanted colon cancer in experimental animals has been studied and their effect has been established on the relationship between the oncogenic and oncosuppressive reactive oxygen species as a key factor in carcinogenesis relevant to the development of effective therapies.

The analytical assessment of the contributions of Assoc. Prof. Nikolova leads to the conclusion of her essential role in enhancing the existing knowledge and theories about electroinduced phenomena in cells, as well as in the development of new hypotheses and approaches for electrotherapy of neoplastic formations. The participation and the contribution of Assoc. Prof. Nikolova in previous applied developments in the Electroinduced and Adhesive Properties Department for successful electrochemotherapy of skin tumours testify for the potential of the candidate for successful participation in the realization of the therapeutic potential of the proposed approaches in practice.

CONCLUSION

The publications and documents presented by Assoc. Prof. Dr. Biliana Pancheva Nikolova-Lefterova meet all the requirements of the Act for the Development of Academic Staff in the Republic of Bulgaria, the Regulations for its implementation and the respective additional institutional regulations at IBPhBME-BAS.

The scientific contributions of the habilitation work and the research achievements of Assoc. Prof. Dr. Biliana Pancheva Nikolova-Lefterova represent advances and developments offering solutions of open scientific problems in the field of electroporation, electrotransmission of macromolecules through membranes and electrochemotherapy of neoplastic formations. The analysis of the presented materials characterizes Assoc. Prof. Nikolova-Lefterova as an established scientist with a clearly defined research profile, significant contribution and a leading role. Hereby, I express my positive assessment of the presented habilitation work and materials together with my conviction in the high scientific value and relevance of the presented research achievements. I strongly support the Scientific Jury to recommend before the Scientific Council of IBPhBME-BAS Biliana Pancheva Nikolova-Lefterova to be appointed the academic position "Professor" in 4. Natural Sciences, Mathematics and Informatics, professional field 4.3 Biological Sciences, Biophysics, for the needs of Electroinduced and Adhesive Properties Department at IBPhBME-BAS.

20 November 2021
Sofia

/Prof. Victoria Vitkova, PhD/