REVIEW

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To the Chairman of the Scientific Jury,
Designated by Order No. RD-38-102/08.02.2022
of the Rector of Sofia University"St. Kliment Ohridski"

Attached please find a REVIEW of the competition for the academic position "PROFESSOR" in the scientific specialty "Medical Physics" in the professional field 4.1 Physical Sciences at the Medical Faculty of Sofia University "St. Kliment Ohridski," announced in State Gazette 103/10.12.2021

with a single candidate

Assoc. Prof. Genoveva Antonova Zlateva, PhD,

Associate Professor, Department of Physics, Biophysics, and Radiology
at Medical Faculty of Sofia University "St. Kliment Ohridski"

I have duly received the electronic form documents and materials required for the competition. The procedure and the conditions for acquiring the academic position "Professor" have been respected and comply with the Academic Staff Development Act in the Republic of Bulgaria, the Regulations for its implementation and the internal regulations of Sofia University "St. Kl. Ohridski".

I declare no conflict of interest, including co-authorship with the candidate.

I. Analysis of the candidate's career profile

Education and qualifications

Assoc. Prof. Genoveva Zlateva graduated in 1987 from the Physics Department of Sofia University "St. Kliment Ohridski" with a degree in Solid State Physics. From 1989 to 1992, she developed her dissertation thesis entitled "Study of phonon structure and cation substitution effects in some superconducting and non-superconducting complex copper oxide systems" at the Department of Condensed Matter Physics at the Physics Faculty of Sofia University "St. Kliment Ohridski", and acquired a Ph.D. degree (at that time "Candidate of Physical Sciences"). In 1999, Assoc. Prof. Zlateva acquired a postgraduate specialty Biophysics, recognized in the health care system.

She speaks English and Russian at a very good and excellent level, respectively, and uses written and spoken German.

Professional experience

Assoc. Prof. Zlateva has a total of 27 years of teaching experience. From 1994 to 2007, she worked at the Department of Physics and Biophysics of the Medical University - Sofia, where she successively held the academic positions of "Assistant Professor", "Senior Assistant Professor," and "Chief Assistant Professor". In 2007 she habilitated and acquired the scientific degree "Associate Professor" in the scientific specialty 01.03.26 "Electrical, magnetic and optical properties of condensed matter" at the Department of Physics, Biophysics, and Radiology at the Faculty of Medicine of Sofia University. Assoc. Prof. Zlateva headed this department for nine years (2010 - 2019). She is currently serving a the second term as Deputy Dean for Academic Activities of the Medical Faculty of Sofia University "St. Kl. Ohridski". In 2019 - 2020 she also held the position of "Director" of the University Quality Management Centre.

II. General characteristics of research activities and assessment of the fulfillment of the minimum national requirements

Assoc. Prof. Zlateva has published **99** full-text publications, in **18**% of which she is the first author and 34% - the second author. The total number of publications in refereed peer-reviewed journals is **38**, and in non-refereed journals - **61**. The total impact factor of the publications is **50.80**, and her individual impact factor is **10.85**. Her publications have been cited **285** times, of

which **215** by *Scopus*. The high scientific significance of the publications of Assoc. Prof. Zlateva is confirmed by her *h-index*, which according to *Scopus*, is **h=7.**

In the competition, without considering the publications for acquiring the academic position "Associate Professor" and Ph.D., Zlateva has submitted **49** publications as follows:

- **19** in refereed and indexed journals in *Web of Science* and *Scopus*, of which **13** papers have an impact factor;
- **30** in non-refereed peer-reviewed journals or edited collective volumes.

The total impact factor of the publications submitted to the competition is **24.15**. Assoc. Prof. Zlateva has participated in **54** scientific forums since taking the academic position of Associate Professor.

In the submitted materials, Assoc. Prof. Zlateva has grouped her scientific papers as follows:

Group A indicators

A.1. Dissertation for the award of Ph.D. – **50 pts.**

Group of indicators B

B.4. Scientific publications in journals that are refereed and indexed in world-known databases of scientific information –**100 pts.** (100 points required)

There are **7** scientific publications in refereed and indexed journals: **2** with **Q1** (2 x 25=**50 pts.**) and **5** with SJR without IF (5 x 10=**50 pts.**).

Group indicators G

G.7. Scientific publications in journals that are refereed and indexed in world-known databases with scientific information, outside the habilitation thesis – **212 pts.** (200 points required)

Twelve scientific publications in refereed and indexed journals were submitted: **2** publications with **Q1** (2 x 25=**50pts.**); **4** publications with **Q2** (4 x 20=**80pts.**); **4** publications with **Q3** (4 x 15=**60 pts.**); **1** publication with **Q4** (**12 pts.**) and **1** publication with SJR without IF (**10 pts.**).

Group indicators D

D.11. Citations in scientific journals, monographs, and collective volumes and patents, refereed and indexed in world-known databases with scientific information – **370 pts.** (100 points required)

There are **185** citations of **19** scientific publications with her participation (185 x 2=**370 pts.**)

Group indicators E– 396 pts.(150 points required)

E.13. Supervision of a successfully defended Ph.D. student – **25 pts.**

E.14. Participation in a national scientific or educational project – **100 pts.**

Assoc. Prof. Zlateva has participated in **10** national projects (10 x 10=**100 pts.**)

E.16. Leadership of a national scientific or educational project – **100 pts.**

Assoc. Prof.Zlateva has led **6** national projects (6 x 20=**120 pts.)**

E.18. Funds raised in projects led by the candidate –**151 pts.**

755943.07 **BGN** were raised under project BG051PO001-3.3.06-0040 (755943.07/5000 = **151 pts.).**

The scientific metrics of Assoc. Prof. Zlateva in some of the groups (**D** and **E**) significantly exceed the minimum requirements for the acquisition of the academic position "PROFESSOR" according to the Regulations for the Implementation of the Law on the Development of Academic Staff in the Republic of Bulgaria and the Regulations on the Conditions and Procedure for Holding Academic Positions at Sofia University "St. Kl. Ohridski".

III. Evaluation of scientific contributions

Assoc. Prof. Zlateva has presented a statement of contributions in 5 main areas, grouped by topic. There are original contributions of scientific and applied nature. All contributions are in the professional field of the present competition.

Some of the more significant contributions arising from the diverse research activities of Assoc. Prof. Zlateva in the five main areas are as follows:

1. Application of redox modulators as cytotoxic agents in tumor cells

- Alpha-tocopheryl succinate (α-TS) has been confirmed to inhibit proliferation and induce cytotoxicity and apoptosis of leukemia lymphocytes without affecting the viability of normal lymphocytes.
- For the first time, the combination of α-TS and some anticancer drugs (barracertib, bortezomib, lonafarnib) has been found to exhibit a strong synergistic cytotoxic effect on leukemic lymphocytes. Moreover, the α-TS - barracertib combination did not exert negative effects, such as oxidative stress and apoptosis, on normal lymphocytes.
- Experimental data with clinical relevance have been obtained: α-TS, in addition to antitumor therapy of acute lymphoblastic leukemia, may contribute to reducing therapeutic doses of the anticancer drugs barazertib, bortezomib, and lonafarnib and to minimizing their side effects.

- α-TS is proposed to be used as a vehicle (matrix) to develop a new generation of drug delivery systems for cancer therapy.
- The combined use of menadione/ascorbate (M/A) was found to have strong cytotoxic effects due to a dose-dependent overproduction of mitochondrial superoxide in isolated glioblastoma cells, but not in normal microglial cells. In comparison, the standard chemotherapeutic temozolomide causes severe oxidative stress in glioblastoma as well as in normal microglial cells.
- It has been hypothesized that the innocuous and even beneficial effect of M/A on normal cells and tissues may be one of the reasons for better tolerability of the drug and lack of adverse effects.

2. **Optical imaging**
   - Highly selective accumulation of quantum dot-labeled polymersomes is demonstrated *in vivo* in models of colorectal cancer.
   - Results have been obtained suggesting that circulating polymersomes serve as carriers that transport drugs to solid tumors, including transportation of small nanoparticles and contrast agents, outlining prospects for the application of polymersomes in the diagnosis and therapy of cancer.
   - Polymersomes labeled with quantum dots due to their high tracking capabilities are suggested to be used as fluorescent probes and nanosystems to transport pharmaceuticals.

3. **Methods and techniques for visualizing pathologies associated with cellular redox status disorders**
   - A two-set sensor system was developed to assess *total antioxidant capacity* (TRC)-QD@CD-TEMPO and determine *oxidative stress level* (OxiStress)-QD@CD-TEMPOH in biological objects using EPR, MRI, and fluorescence optical imaging.
   - Evidence is presented regarding the high sensitivity and resolution of the developed sensor system, which may allow for functional diagnostics of physiological processes unrelated to macro anatomical structure changes. Only one study was published with a QD@nitroxide-based probe developed for redox status visualization.
   - It was found that intracellular access, in particular mitochondrial access, is achieved by using the developed two-set sensor system since the sensors are composed of quantum dots coated with multinitroxide-functionalized cyclodextrin conjugated with triphenylphosphonium groups.

- TRC sensor was demonstrated to detect low levels of redox imbalance caused by ROS overproduction using contrast-enhanced MRI.
- Results were obtained showing that hypercholesterolemia induces oxidative stress in the kidney of experimental models, and this process can be visualized using the redox-sensitive mito-TEMPO magnetic resonance contrast probe. Reasons are stated for clinical application of the obtained results in early diagnosis of renal dysfunction based on the redox state of renal tissues.
- An algorithm is proposed for extracting contrast-enhanced signals from MRI images using the open-source *ImageJ* script software. Thus, it is possible to assess the degree of functional impairment based on tissue redox status and the dynamics of contrast changes.

4. **Investigation of surface and interface polariton modes of optical phonons (SPP and IPP) in low-dimensional structures**
   - Raman spectra of samples representing Si matrix with ion-implanted nanolayers of semiconductor β-$FeSi_2$ and Mg_2Si silicides, as well as Raman and IR spectra of InN nanofilms on a buffered AlN nanolayer deposited on a sapphire substrate were studied.
   - Different spectral features resulting from the generation of surface and interface phonon-polariton (SPP and IPP) modes are interpreted.

5. **Increasing the quality of medical students' education**
   - Various educational forms and methods are proposed to increase the motivation of medical students to learn and achieve higher results in physics and other core subjects. The role of game-based pedagogical technologies and the creation of interdisciplinary teaching modules covering general medical problems solved by the joint efforts of specialists in medical physics, pathology, physiology, etc., are discussed.
   - It is proposed to create a terminology guide to improve the quality of education of foreign medical students studying in higher education institutions in Bulgaria.

Assoc. Prof. Zlateva was the supervisor of 1 successfully defended Ph.D. student whose thesis was entitled "Contrast-enhanced magnetic resonance imaging techniques to visualize pathologies associated with cellular redox status disorders."

IV. Participation in educational and scientific projects

Assoc. Prof. Genoveva Zlateva has participated in a total of **21** educational and scientific projects. She has led **7** of these projects, one of which is a European project under the Human

Resources Development Operational Programme (BG051PO001-3.3.06-0040), and is entitled "Building interdisciplinary teams of young researchers in basic and applied research relevant to medical practice".

During the implementation of the project, funds amounting to 755 943.07 BGN were attracted. Assoc. Prof. Zlateva was also the coordinator of a bilateral project between St. "Kl. Ohridski", Faculty of Medicine, and the National Institute for Radiological Research of Japan (contract No. 394/2017). Two research projects with her participation were funded by the Medical Science Council at the Medical University of Sofia; 14 - by the Research Fund at Sofia University. "Kl. Ohridski", 1 - by the "Scientific Research" Fund of the Ministry of Education and Science (RNF01/0107) and 1 - by a consortium of 3 scientific organizations, including the "Scientific Research" Fund of the Ministry of Education and Science (D-01-835/07). Two projects were related to teaching activities: the European project BG051PO001-3.3.06-0040 led by her and the Student Practices - Phase 1 (BG05M20P001-2.002-0001), in which she acted as an academic mentor.

V. Teaching and Learning Activities

Assoc. Prof. Zlateva has presented a report on her teaching workload for the last five years, showing teaching activity significantly exceeding the load assigned to a habilitated lecturer at St. "Kl. Ohridski". Her teaching load averages 731.9 academic hours, of which 584.5 academic hours are classroom and 147.5 academic hours are extracurricular. She has taught courses in "Physic" and "Biophysics" for the needs of the specialty of "Medicine"; "Medical Instrumentation in Nursing Practice" for the needs of the specialty of "Nursing"; and "Biomechanics" for the needs of the specialty of "Medical Rehabilitation and Occupational Therapy". She has conducted 225 lecture hours and 495 classroom hours in Physics and Biophysics in English with international medical students at the Medical Faculty of Sofia University for the last five years.

VI. Expertise

Assoc. Prof. Zlateva has been a reviewer of publications in reputable journals (Chinese Journal of Cancer Research; Int. J. Automat., J. Exp. Clin. Medicine, Bulg. J. Phys), as well as research projects under the Scientific Research Fund of the Ministry of Education and Science. She has been the chair of expert groups for accreditation of doctoral programs at NAOA in "Medical Physics" (MU-Varna, 2016);"Medical Physics" (St. Konstantin Preslavski University, 2018).); "Biophysics" (MU-Sofia, 2018) and "Medical Physics" (Trakia University, 2021), and

member of the expert group for accreditation of the doctoral program at the NAOA "Medical Biophysics" (MU-Pleven, 2021).

Assoc. Prof. Zlateva has participated as a member or chairperson of scientific juries for the acquisition of the degree of Doctor - **1**; Ph.D. - **4**; the academic position of Associate Professor – **3;** and Professor - **2**.

CONCLUSION

There is a single candidate – Assoc. Prof. Genoveva Antonova Zlateva in the competition for the academic position "PROFESSOR" in the scientific specialty "Medical Physics" at the Department of Physics, Biophysics, and Radiology at the Medical Faculty of Sofia University "St. Kliment Ohridski"

I highly appreciate the extensive teaching and research activities of Assoc. Prof. Zlateva. She is an erudite lecturer and scientist, actively implementing new approaches and technologies to improve the learning process. Assoc. Prof. Zlateva is thoroughly familiar with and uses various biophysical and biochemical research methods. Her research is of high level and has found a comprehensive response in the scientific literature. She has valuable original contributions of scientific and fundamental nature.

Studies of Assoc. Prof. Zlateva have been published in the most renowned scientific journals with impact factor. Many researchers in reputable foreign journals have cited them. Assoc. Prof. Zlateva is a sought-after reviewer of publications and scientific projects.

All the documents submitted by Assoc. Prof. Zlateva for the competition, including materials concerning her scientific and teaching activity, meet all the requirements of the Academic Staff Development Act in the Republic of Bulgaria, the Regulations for its implementation, and the internal regulations of Sofia University "St. Kl. Ohridski". Her scientific metrics significantly exceed the minimum national requirements for the acquisition of the academic position "PROFESSOR".

I strongly recommend the honorable members of the Scientific Jury vote to award Assoc. Prof. Genoveva Antonova Zlateva to the academic position "PROFESSOR" in the scientific specialty "Medical Physics", professional field 4.1 Physical Sciences at the Faculty of Medicine of Sofia University "St. Kliment Ohridski".

28.03.2022 Reviewer:

Pleven /Prof. M. Alexandrova, D.Sc./