Review

on the materials submitted for participation in a competition for the academic position of "Professor" in the Field of higher education 4. "Natural Sciences, Mathematics and Informatics", Professional field 4.2. "Chemical Sciences" (Theoretical Chemistry - Computational Chemistry), announced in State Gazette, no. 21 from 15.03.2022 for the needs of the Faculty of Chemistry and Pharmacy at Sofia University "St. Kl. Ohridski "

Reviewer: Prof. Dr. Natasha Trendafilova, IGIC-BAS

The only candidate in the current competition for the academic position of "Professor" in the Professional field 4.2. "Chemical Sciences" (Theoretical Chemistry - Computational Chemistry) is **Assoc. Prof. Dr. Galia Kostova Madjarova**, ORCID: 0000-0002-6786-2719, Scopus Author ID: 6602638896, Web of Science ResearcherID: A-9124-2013.

The documents submitted by the candidate are in compliance with the requirements of the Law for development of the academic staff in Republic of Bulgaria and the Regulations for its implementation, the Regulations for the terms and conditions for acquiring scientific degrees and holding academic positions at Sofia University "St. Kl. Ohridski", as well as with the Recommended Criteria of the Faculty of Chemistry and Pharmacy, Sofia University, for acquiring scientific degrees and holding academic positions for professional field 4.2. "Chemical Sciences".

The reference for the fulfillment of the minimum national requirements under art. 2b (2) of the Law for development of the academic staff in Republic of Bulgaria, as well as with the Recommended Criteria of the Faculty of Chemistry and Pharmacy, Sofia University, in Professional field 4.2. "Chemical Sciences", for academic position "Professor", shows that Assoc. Prof. Dr. Madjarova fulfills and even exceeds the required minimum.

Assoc. Prof. Dr. Galia Madjarova has graduated from the Faculty of Chemistry at Sofia University "St. Kl. Ohridski" in 1995 with a Master's degree in "Chemistry" and a specialization in "Chemical Physics and Theoretical Chemistry". In 1999, after successfully defending her dissertation at the Faculty of Chemistry at Sofia University, Galia Madjarova was awarded the educational and scientific degree of "Doctor" in "Theoretical Chemistry". In the period 2001-2013, she was elected successively as "Assistant" (2001-2002), "Senior Assistant" (2002-2005) and "Chief Assistant" (2005-2013), and since 2013 she has held the academic position "Associate Professor" in "Theoretical Chemistry" at the Faculty of Chemistry and Pharmacy at Sofia University. Simultaneously with the intensive research work, Assoc. Prof. Dr. Madjarova is a lecturer in Structure of Matter (1998-), Theoretical Chemistry (2003-2018), Molecular Design (2003-), Molecular Modeling of Functional Materials (2012-), Quantum Chemistry and Molecular Mechanics (2016-), Quantum Chemistry and Spectroscopy (1998-2009) (for bachelors) and Applied Computational Chemistry (for masters).

Assoc. Prof. Dr. Madjarova has conducted a number of successful and important for the formation of her scientific profile specializations: 5 short-term research visits at the University of Leipzig, Germany (1996-1999), Post-doc at the Institute for Fundamental Chemistry, Kyoto, Japan (2000-2001), STSM at the Institute for Chemistry of Surfaces and Interfaces, Mulhouse, France (2004),

RS Incoming Short Visit Grant at the University of Hull, Hull, UK (2005) and guest researcher at the Max Planck Institute of Microstructure Physics, Halle (Saale), Germany (2014-2015).

An integral part of the research and teaching activity of Assoc. Prof. Madjarova is her active participation in research projects: 12 national and 2 international, she was the leader of 6 projects funded by the Research Fund of Sofia University. She is currently co-head of the Laboratory for Modeling and Forecasting of Processes and Properties of Clean Technology Materials at the National Center for Mechatronics and Clean Technologies. In the period 2001-2012, Assoc. Prof. Dr. Madjarova was a scientific consultant for 6 master's theses and 1 PhD thesis, reviewer of 5 master's theses, worked with students in the Laboratory of Quantum and Computational Chemistry. Since 2012 she has been the research supervisor of 2 bachelor's and 2 master's theses and the co-supervisor of 1 PhD student.

In the recent years, Assoc. Prof. Dr. Madjarova has been actively involved in the academic life and in the management of Faculty of Chemistry and Pharmacy, Sofia University. Her administrative engagement includes: Deputy Dean for Pharmacy and Postgraduate qualification (since 2019), Member of the Faculty Council of the Faculty of Chemistry and Pharmacy, Chairman of the Academic Council of specialty “Pharmacy”, Member of the General Assembly of Sofia University, member of the University Training Commission of Sofia University, head of the Department of Physical Chemistry and Molecular Modeling for the specialty “Chemistry”.

For participation in the current competition for the academic position "Professor", Assoc. Prof. Dr. Madjarova presents one published monograph on "*Design of new solid magnetic materials without the use of rare earth elements*" (University Press “St. Kl. Ohridski”, 2022) and 11 original scientific papers that were not included in her "Doctor" thesis (1999) and in the competition for “Associate professor” at Faculty of Chemistry and Pharmacy at Sofia University (2012). All scientific publications, as well as the monograph, are in line with the topic of this competition - Theoretical and Computational Chemistry. The articles are published in refereed journals with impact factor and quartile, of which 9 (82%) are in journals of category Q1, 1 in Q2- and 1 in Q4 journal). At the time of application, 86 citations (*Scopus*) have been noticed on these publications. The total number of publications of the candidate is 41, the total number of citations is 331 and the Hirsch index according *Scopus* is 12.

In the focus of the theoretical research of Assoc. Prof. Dr. Madjarova are the structure and properties of important for the practice systems, described through theoretical models and studied by the methods of the computational chemistry. The research is characterized by depth and innovation and consists in: *(i)* the successful application of atomistic MD simulations to study the supramolecular structural organization of biological structures and the mechanisms of connection of active drug delivery systems, *(ii)* in the skillful application of quantum chemical methods to model the properties of magnetic systems, membranes for gas separation and excitation processes as well as in *(iii)* the innovative application of machine learning methods to study the “composition-structure-properties” relationship in magnetic structures.

In connection with the possibility of drug delivery and food applications, the inverted hexagonal mesophase composed of glycerol monoolein (GMO), tricaprin and water has been studied in detail.

The lipid-lipid arrangement and that at the water-lipid interface are described by statistical analysis of the data obtained from trajectories in MD simulations. Statistically meaningful and very contrast images of the radial mass density distribution were obtained, which show a hexagonal shape at the monoolein/water interface. It was found that water interacts with the headgroups and forms a three-layer diffusive mass density distribution. The shape of each layer is found to be close to hexagonal and suggests long-range interactions. It has been found that water molecules that are located at the water/lipid interface are characterized by very intense dynamics and few of them are hydrogen bonded to the monoolein heads.

The study has been expanded with addition of tricaprylin. The resulting system was studied in the presence and absence of lysozyme. Lysozyme entrapment has been found to cause local disturbances in the lipid structure, but does not alter the behavior of the model systems, while the secondary structure of the peptide is strongly influenced by the insertion and an optimal lipid tube radius should be sought to minimize disturbances. A tube of optimal size for protein transport with minimal perturbation of its secondary structure is proposed.

In another innovative study, Assoc. Prof. Dr. Madjarova studied in detail the factors responsible for the formation of primary micelles from salts of bile acids. The structure of the aggregates obtained in the course of molecular-dynamic simulations is correctly and exhaustively described. The influence of the number of hydroxyl groups in the sterol fragment on the formation of aggregates has been established. Hydrophobic interactions have been shown to be the main stabilizing force of the primary micelles, and the formation of hydrogen bonds accelerates the aggregation of taurine and glycine-modified salts. It is important to note that the results are in very good agreement with experimental data as the simulations were performed under conditions close to those in the human gastrointestinal tract.

Special attention should be paid to the in-depth research of Assoc. Prof. Dr. Madjarova, dedicated to the modeling of components of system for active transport of drugs based on folate or antifolates in combination with α-folate receptor (FRα). By studying the structure of 6 targeting ligands in saline (folate, 5-methyltetrahydrofolate, raltitrexed, pemetrexed, methotrexate and pteroyl ornithine), a significant population of *cis*-isomers was found by the amide bond as well as with an order of magnitude faster structural dynamics of *trans*-isomers in all ligands. The results showed that despite the structural diversity in the liquid medium, the molecular area available for interactions with water molecules is almost constant. The predominant tautomeric form of the folate in solution was determined. Theoretical and experimental data have predicted rapid proton exchange between the N1 and N3 positions of pterin. An important contribution is the atomistic model of a neoplastic cell membrane (based entirely on experimental data) proposed for the first time in the literature, which describes in depth and details the interaction of ligands with the α-folate receptor (FRα). The influence of the methods of pressure scaling on the results of the simulations has been studied. Spontaneous binding of three ligands (folate, raltitrexed and 5-methyltetrahydrofolate) to the active site of the receptor was observed with this model.

The TDDFT formalism, which uses a “bootstrap kernel” and successfully describes the exciton nature of excitation, has been applied to calculate the dielectric function of three molecular crystals

(picene, pentacene and 1D-polymer poly(p-phenylenevinylene)). This formalism is proposed for rapid estimation of the excitation spectra of different materials.

Numerous results, obtained during the modeling of the magnetic properties of permanent magnets without rare earth elements in the structure, are described in detail in two scientific articles and in the published monograph. The focus of the research is on the magnetic properties of Heusler alloys and the possible tetragonal and hexagonal deformations, the spontaneous magnetization and the energy of the magneto-crystalline anisotropy. The construction of stacks of existing binary magnets of FePt, MnAl and MnGa is modeled in order to increase the magneto-crystalline anisotropy of the formed L10 structure. These studies are particularly relevant as they relate to the search for new solid magnets without rare earth elements in the structure, which are important for the purposes of the carbon-neutral economy.

The monograph, which is written on 92 pages and cites 74 literature sources and websites, provides a comprehensive overview of the magnetic materials used in the practice, presents the main characteristics of permanent magnets and outlines the possibilities for quantum chemical modeling and theoretical forecasting. The idea of studying the phase space of Heusler alloys has been expanded with an emphasis on the hexagonal structure as a potential candidate for the production of permanent magnets with a large magneto-crystalline anisotropy. The factors influencing the basic magnetic characteristics have been identified.

An important contribution in these studies is the proposed 14 parameter model, which allows to predict qualitatively and semi-quantitatively the total magnetic moment of the elementary cell of any structure composed of d-, p- and part of the f-elements with known volume. Parameters, closely related to the individual characteristics of the atoms, such as electron affinity, ionization potential, electronegativity, number of valence electrons and covalent radius, were selected. With this research, Assoc. Prof. Dr. Madjarova convincingly shows the possibility of applying machine learning in materials science and in particular in the field of magnetic materials.

The author's reference of Assoc. Prof. Dr. Madjarova describes in detail the specific motivation and course of the research, the most important results and conclusions from them, and clearly outlines the candidate's own contributions. They consist in the development of original and physically correct theoretical models for conducting atomistic MD simulations of the supramolecular structural organization of biological structures, for studying the spontaneous aggregation of bile acid salts in aqueous solution, as well as for studying the binding mechanisms of active drug delivery systems. Contributions to the research are also the numerous results and theoretical dependences obtained in the quantum chemical modeling (TDDFT) of the magnetic properties of permanent magnets without rare earth elements in the structure and in the calculation of the excitation spectrum of molecular crystals and 1D polymers. Important correlations "composition-structure-properties" have been established through the successful application of machine learning methods.

The analysis of the conducted theoretical research gives the impression that Assoc. Prof. Dr. Madjarova is an in-depth researcher with innovative ideas, for the solution of which she competently applies a wide range of computational methods and algorithms. The research

described in the publications impresses with exceptional depth and comprehensiveness, as well as with numerous valuable theoretical results. The latter are correlated with data from specific experiments, which makes the conclusions correct and convincing. When reviewing the publications and the monograph, I did not find any plagiarism.

**Conclusion.** In the competition for the AP "Professor", Assoc. Prof. Dr. Galia Kostova Madjarova presented one published monograph and sufficient number of scientific papers after the defense of the "Doctor" thesis and the occupation of the AP "Associate Professor". The scientific papers are published in authoritative international journals with a high impact factor and quartile, which is a proof of their high quality and international recognition. The candidate's research has original scientific and methodological contributions, as well as many valuable results. Given the high scientific level and the volume of the research, the scientometric and biographical data of the candidate, I confidently vote "yes" to this, Assoc. Prof. Dr. Galia Kostova Madjarova to take the academic position "Professor" in the professional field 4.2. "Chemical Sciences" (Theoretical Chemistry-Computational Chemistry) in Faculty of Chemistry and Pharmacy at Sofia University.

Reviewer:

Sofia, 29.06.2022 (Natasha Trendafilova, Prof. Dr., IONH-BAS)