OPINION

by Assoc. Prof. Miroslav Angelov Rangelov, PhD

Institute of Organic Chemistry with Centre of Phytochemistry (IOCCP), Bulgarian Academy of Sciences (BAS)

Concerning the materials submitted for the competition for academic position "Associate Professor" within the Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Science (IOCCP-BAS) in professional field 4.2 Chemical Sciences: scientific specialty "Organic Chemistry" for the needs of the Laboratory "Structural Organic Analyses"

1. Evaluation of the documents in the procedure

According to order № RD-09-127/23.06.2025 of the Director of IOCCP-BAS, I have been approved as a member of the academic board in connection with a procedure for a competition for the academic position of "Associate Professor" for the needs of the "Structural Organic Analyses" laboratory, announced in the Newspaper of State, issue 40 of 16.05.2025. The only candidate participating in the competition is Senior Assist. Prof. Simeon Stoyanov Stoyanov, PhD. The set of materials presented by the candidate is in accordance with the Regulations for the Development of the Academic Staff of the IOCCP-BAS and meets the criteria of IOCCP-BAS for academic positions " Associate Professor"

Dr. Simeon Stoyanov participates in the competition with a 24 scientific work outside his thesis for "Doctor", which are on the issues of the competition and are accepted for review:

- Publications equivalent to habilitation report (Indicator C) – 9 pieces, divided by the relevant Q factors as follows: - Q1 - 3 pcs., Q2 - 2 pcs., Q3 - 1 pc., Q4 - 3 pcs.
- Publications outside the equivalent of habilitation report (Indicator D) – 15 pieces, divided by the relevant Q factors, as follows: Q1 – 3 pcs., Q2 - 6 pcs., Q3 - 2 pcs., Q4 - 4 pcs.

Dr. Simeon Stoyanov holds 119 citations of his scientific publications.

A check in the Scopus database shows that Dr. Stoyanov holds an h factor of 6 , which meets the criteria of the IOCCP-BAS for the academic position.

The results of the investigations are presented at 32 national and international forums such as poster presentations and oral reports. Dr. Stoyanov has presented participations in 14 scientific research projects.

The presented articles as a number, as an impact factor and citations, meet the requirements set by IOCCP-BAS for holding the position of "Associate Professor".

The articles presented meet the requirements set by the IOCCP-BAS for the position of "Associate Professor." The points by indicator groups for the academic position of "Associate Professor" are as follows: 166 points for indicator C, 273 points for indicator group D, and 238 points for indicator group E. The points for all indicators exceed the required minimums.

2. General characteristics of the candidate's research activity

The candidate's scientific interests are mainly focused on the study of the organic anionic derivatives – carb-, azo-, and oxyanions through a combined experimental-theoretical approach to the interpretation of their vibrational spectra.

The contributions of the research activity of Dr. Stoyanov are summarized in five main areas - (1) Prediction of nitrile frequencies and intensities observed in molecules, anions and radicals based on ab-initio and DFT, (2) Application of DFT and solvation models to describe the spectral and structural changes induced by the conversion of substituted benzophenones into ketyl radicals, (3) Vibrational spectra and structure of carbanion derivatives, (4) Vibrational spectra and structure of oxy- and azanion derivatives, (5) Vibrational spectra and structure of anionic and radicalanionic derivatives of nitroaromatic compounds.

1. First field of research established specialized scaling factors and equations to improve the accuracy of theoretical predictions for nitrile stretching frequencies and intensities in molecules, anions, and radicalanions. After identifying a systematic underestimation of nitrile frequencies, the study calculated scaling factors for 11 basis sets using B3LYP. For closed-shell molecules and anions, the best results were achieved with basis sets containing diffuse functions. For radicalanions, the optimal balance of accuracy and computational efficiency was found with the B3LYP/6-311+G level, noting that "triple zeta" basis sets are generally preferable for radicals. Since predicting nitrile intensities is more challenging than predicting frequencies; it is mentioned that ab initio methods outperformed DFT, and basis set expansion did not improve results. A key overall conclusion is that the use of basis sets with diffuse functions is essential for accurately simulating these IR spectra.
2. Second field of study addressed the challenge of accurately predicting the significant decrease in carbonyl frequencies when substituted benzophenones are converted to their radical anions using DFT. After testing various functionals, a mixed ONIOM-IEFPCM solvation model was identified as a highly effective compromise between accuracy and computational cost. This advanced approach dramatically improved the results, reducing the MAD between theoretical and experimental carbonyl frequencies from 31 cm^{-1} to an excellent 4-6 cm^{-1}. The model was deemed successful as it adequately describes the molecular structure, conjugation, and functional group polarizability, and it was subsequently used to analyze structural changes in bond lengths, angles, and electron density distribution upon radical anion formation.
3. Third field of study investigates the relationship between the structure of various carbanions and their vibrational IR spectra. The studies demonstrate that increasing the number of adjacent carbanion centers on a molecule, such as in tetracyanopropane, causes a significant and cumulative decrease in nitrile stretching frequencies due to inductive and mesomeric effects. Furthermore, the isomerization of carbanion adducts shows that increased charge delocalization leads to a slight increase in nitrile frequencies. For the pharmaceutical compound phenindione, deprotonation to its carbanion results in a major structural change to a planar form and a large decrease in carbonyl frequencies, with the charge being highly delocalized and stabilized across the molecular framework. In all cases, excellent agreement was found between the experimental IR data and theoretical calculations, validating the computational models for predicting structural changes, and charge distribution upon carbanion formation.
4. Forth field of study employs experimental IR spectroscopy and DFT calculations to characterize the structure and vibrational spectra of biologically relevant oxyanions and azanions. For the antioxidant apocynin, theoretical calculations identified its preferred radical scavenging mechanisms (HAT in lipophilic media, SPLET in hydrophilic media) and the IR spectrum of its key intermediate oxyanion was experimentally validated. Similarly, the anions of pharmaceutical compounds acedobene and salophene were synthesized, and their IR spectra showed systematic shifts in characteristic bands upon deprotonation; these changes were accurately predicted by theory, with excellent agreement between calculated and experimental spectra. Structural analyses revealed significant changes in bond lengths, angles, and charge distribution upon anion formation, providing key insights into the electronic structure and stability of these pharmaceutically important species.
5. Fifth field of study investigates the vibrational spectra and structure of anionic and radical anionic derivatives of nitroaromatic compounds, which are crucial for understanding the biological activity and toxicity of many pharmaceuticals. Experimental IR and Raman spectroscopy, combined with DFT calculations, revealed that the formation of radical anions consistently causes a decrease in nitro group frequencies and a significant increase in the C-NO_2 stretching frequency. For all studied compounds (including various nitrobenzimidazoles, nimesulide, and flutamide), the spin density of the radical anion was found to be predominantly localized on the nitro group (>70%), and the most significant structural changes occurred in the nitro group and the adjacent heterocyclic ring. The theoretical data excellently matched the experimental spectra and provided key electronic parameters (reduction potentials, HOMO-SOMO energies, electron affinities) to quantify and

compare the nitroreduction propensity of these compounds. This work establishes a strong structure-spectra-activity relationship, showing that the cytotoxicity of these drugs under hypoxic conditions is directly linked to the formation of these radical anions.

3. Critical notes and recommendations
I have no critical comments or recommendations.

CONCLUSION
The documents and materials presented by Dr. Simeon Stoyanov Stoyanov fully comply with the requirements of the Act for the development of the academic staff in the Republic of Bulgaria, The Regulations govern the implementation of the Act for the development of the academic staff in the Republic of Bulgaria, and meets the criteria of IOCCP-BAS for academic positions "Associate Professor". Based on the materials presented in the competition and the scientific and scientific-applied contributions reflected in them, I give my positive assessment and recommend to the other members of the Scientific Jury that a report-proposal be prepared to the Scientific Council of IOCCP for conferment of the academic position "Associate Professor" of Dr. Simeon Stoyanov Stoyanov in professional direction 4.2. "Chemical Sciences", scientific specialty "Organic Chemistry" for the needs of the laboratory "Structural Organic Analyses".

24.09.2025

Assoc. Prof. Miroslav Rangelov, PhD