INSTITUTE OF MACROMOLECULAR CHEMISTRY
CZECH ACADEMY OF SCIENCES

Dr. Ognen Pop-Georgievski
Dpt. Chemistry and Physics of Surfaces and Interfaces
Tel: +420 296 809 340
Fax: +420 296 809 410
E-mail: georgievski@imc.cas.cz

Review of doctoral thesis:

"Responsive Polymer Materials: From Light- to Thermo- and Redox-Responsive Systems"

submitted by Ing. Pavel Švec

The dissertation thesis submitted by Ing. Pavel Švec focuses on the synthesis and systematic study of polymer materials designed to respond to physical and chemical stimuli, targeting drug delivery applications. The key achievements of submitted thesis present the of new conjugable pyrazinacenes showing promise a for the development of polymer based upconversion materials; the development of the first controlled polymerization of (2-nitrobenzyl)acrylate (NBA) and synthesis of polyNBA-based copolymers that disassemble under stimuli such as UV light; and the introduction of pH-, thermo-, and redox-responsive fluorinated polymers for 19F MRI imaging. In addition, the thesis presents fluorinated ferrocene derivatives to create redox-responsive polymer sensor systems traceable by 19F MRI and studies the properties of various gradient copolymers based on 2-aryl-2-oxazoline monomers for the design of drug delivery systems.

The thesis consists of abstract, introduction, aims, results and discussion part summarizing the obtained main results and conclusions. The submitted thesis has 109 pages and references the 6 main publications (2 published as first author) referenced as appendixes from which it mainly sources. The work is well concepted and organized with a clear presentation and vision. The introduction provides a very careful resume on the development in the field bridging academia research and commercial products/applications present on the market. The candidate addresses and explains all obtained results independently going well beyond his published works. I highly value the fact that the candidate explains the chosen synthesis procedures/polymerizations and pick-points the downfalls of some of the utilized concepts and presented avenues. I find this as a great instructive benefit for the new-commers in the field.

Despite the fact that the work is rather precisely written, I have to point out few discrepancies, typos and inconsistencies:

i) Page 25, missing space in: "superoxide radicals ($^{\bullet}O_2^-$),hydrogen peroxide (H_2O_2)";
ii) Author uses well defined polymer length, instead of polymerization degree;
iii) Page 27, author uses well defined polymer length, instead of polymerization degree;
iv) Inconsistent using of symbols for radicals (Example Page 29–30 and 25);
v) Within the Aims of thesis section, the specific aim 4 lacks a notation of the individual designation of sub-aims.
vi) Parts of the results and discussion elaborate the R_h while others D_h, this could have been unified;
vii) Minor stylistic issues in Table 3 and Table 4;
viii) Missing adverb on Page 84, sentence: "…We choose…. We chose the antibiotic drug rifampicin (log D = 1.3) ^{300} the model compound.", missing "as";
ix) The thesis precisely references/numbers the synthesized compounds through out the work, however, I think it would have beneficial to have a table or list of compounds similarly to the List of abbreviations.

However, the pointed-out discrepancies, typos and inconsistencies are minor and do not seriously affect the quality of the dissertation. As previously noted, the thesis mainly builds on 6 publications (2

published as first author) of a high scientific visibility. In addition, the applicant (co-)authored 12 publications and was involved in 2 patents which have not been part of the thesis. In my opinion the applicant has shown a high level of independence, diligence and creativity, thus undoubtedly demonstrating to be fully capable of performing independent research. As to date when this thesis review is being submitted the applicant has achieved a Hirsh index of 10 (according Scopus, Total number of citations: 260, Documents: 18).

At the end I would like to express my agreement with the Applicant's concluding remark, that his **dissertation provides valuable insights and methodologies for future improvements in responsive polymer systems**.

Therefore, I **strongly recommend Ing. Pavel Švec´s dissertation for defense at the Chair of Macromolecular Chemistry, Faculty of Science, Charles University.**

Specific questions to the dissertation:

1) The candidate shares and explains possible drawbacks on the EPR effect. Can he further elaborate them? Can the author give a critical view on future implementation of drug delivery systems?
2) The candidate uses the term "living" radical polymerization, can he comment on the correctness of this term?
3) Within the discussion can the author further explain the differences of the concepts of SET-LRP and SARA-ATRP? Which is the most term should be used for Cu(0)-mediated Reversible Deactivation Radical Polymerization? Can you comment and give your critical opinion on the Percek/ Matyjaszewsky debate?
4) Are the synthesized phenanthroline-fused pyrazinacenes selective towards complexation of Ru^{2+} ions?
5) Figure 10, panel C. Can the Author further explain the discrepancies between the measured D_h values in PBS and water. Can he elaborate the supposed UV crosslinking?
6) Figure 14 reports high fluctuations of MRI signal within individual series and high errors. Can you further address this issue?
7) Page 86: "The PhOx copolymers formed spherical micelles with diameters similar to those obtained by DLS (Figure 28). However, the diameters detected by TEM were smaller than the diameters obtained by DLS which is caused by polymer shrinkage in its dry state (trehalose does not completely prevent the deformation of the NPs upon dehydration). Furthermore, DLS systematically overestimates NPs diameter because of the hydration layer."
   Can the candidate comment of what is meant with the overestimation of the diameter?

In Prague, 29.08. 2024

Ing. Ognen Pop-Georgievski, Ph.D.
Department of Chemistry and Physics of Surfaces and Biointerfaces
Institute of Macromolecular Chemistry, Czech Academy of Sciences
Heyrovského nám. 2
162 06 Prague 6

INSTITUTE OF MACROMOLECULAR CHEMISTRY, CZECH ACADEMY OF SCIENCES
Heyrovského nám. 2, 162 06 Prague 6, Czech Republic, tel.: +420 296 809 111, e-mail: office@imc.cas.cz, www.imc.cas.cz