Skoltech
Skolkovo Institute of Science and Technology

Jury Member Report – Doctor of Philosophy thesis.

Name of Candidate: Yuliya Kan

PhD Program: Materials Science and Engineering

Title of Thesis: Development of core-shell fiber composite based on polyvinyl alcohol modified with graphene oxide and silica for biomedical applications

Supervisor: Professor Alexander Korsunsky

Name of the Reviewer:

I confirm the absence of any conflict of interest (Alternatively, Reviewer can formulate a possible conflict)	**Date: 11-12-2022**

The purpose of this report is to obtain an independent review from the members of PhD defense Jury before the thesis defense. The members of PhD defense Jury are asked to submit signed copy of the report at least 30 days prior the thesis defense. The Reviewers are asked to bring a copy of the completed report to the thesis defense and to discuss the contents of each report with each other before the thesis defense.

If the reviewers have any queries about the thesis which they wish to raise in advance, please contact the Chair of the Jury.

Reviewer's Report

Reviewers report should contain the following items:

- Brief evaluation of the thesis quality and overall structure of the dissertation.

  In this work, the candidate fabricated core-shell fibbers composite or biomedical applications by using the coaxial electrospinning technique. Several experiments were designed to characterize the fabricated core-shell fibre mats and plentiful and massive quantified data were measured and presented. Also, the candidate has published her results in several nice academic journals under professional reviewers from all over the world, so I do not have too much concern about the data and results done by you.

- The relevance of the topic of dissertation work to its actual content.

  The thesis title matches the research topic and results.

- The relevance of the methods used in the dissertation.

The candidate utilized plentiful equipment to assist and study her research experiments and massive quantified data were measured and presented in this thesis. All utilized techniques and methods are satisfied with her research topic and needed.

- The scientific significance of the results obtained and their compliance with the international level and current state of the art.

  The candidate has published her results in several nice academic journals under professional reviewers from all over the world, so I do not have any concerns about the data and results done by you. I believe that this research quality achieves a high international standard.

- The relevance of the obtained results to applications (if applicable)

  The results have a high potential to be transferred as a commercial product in the biomedical field.

- The quality of publications

  As mentioned, the candidate has published her results in several nice academic journals so that her thesis achieves a high standard and quality in the biomaterials field and applications.

The summary of issues to be addressed before/during the thesis defense.

There's plenty of room at the bottom and I would like to encourage the candidate to address more connections between each measured result accomplished with fundamentals and theories. Then, readers could learn from your academic contributions and discoveries. Otherwise, after reading it, I only obtained and learned about so much data that you measured and so many tools you utilized and only presented in this thesis. Moreover, all presented data must be accurate and precise because of a standard required by an academic manuscript so please carefully recheck all data in the whole thesis again. I attached a file with my comments and viewpoints for her reference. I believe that the candidate could answer all questions in the defense meeting and welly revise and recognize her thesis perfectly.

PS. Please see the attachment about my suggestions and viewpoints.

Provisional Recommendation

☑ *I recommend that the candidate should defend the thesis by means of a formal thesis defense*

☐ *I recommend that the candidate should defend the thesis by means of a formal thesis defense only after appropriate changes would be introduced in candidate's thesis according to the recommendations of the present report*

☐ *The thesis is not acceptable and I recommend that the candidate be exempt from the formal thesis defense*

THESIS TITLE:

DEVELOPMENT OF CORE-SHELL FIBER COMPOSITE BASED ON POLYVINYL ALCOHOL MODIFIED WITH GRAPHENE OXIDE AND SILICA FOR BIOMEDICAL APPLICATIONS

ABSTRACT:

The abstract section provides comprehensive research details and summarizations of all experimental results. But there are certain typing and grammar mistakes and please revised them.

SELF PUBLICATIONS (page 6):

Please reorganize the format of each publication list, such as page number.

FELF-PUBLISHED CONFERENCE PAPERS (page 7):

Also, please recheck the format of each published conference paper.

LIST of FIGURES:

Please modify some descriptions and provide more information for figures not only in the part but also in the context.

LIST of TABLES:

If more descriptions could be accompanied by the tables, it should be more friendly for readers to quickly enter the same field.

ACTUALITY and PROBLEM STATEMENT (Chapter 1)

Normally, the first chapter should descript the research purpose and targets for the current needs but there is no plentiful information and statement about why and how to match and satisfy the requirements and standards, especially for medical applications as mentioned in the title of this thesis, after reading this chapter. Therefore, readers are keen to clearly obtain the research challenge that could be conquered, standards must be reached, techniques might be utilized, contributions would be proved, and discoveries should be achieved from this thesis and research. Therefore, I recommend that this chapter could be reorganized and current medical needs with challenges and technical difficulties of fibrous scaffolds should be emphasized and listed on pages 20 and 21, if possible. Otherwise, we only catch the materials prepared and techniques and equipment selected in the current section.

1. I personally get stuck, when reaching the last paragraph of chapter 1. The last paragraph is valuable to be addressed in this thesis, but the location is unsuitable, and the information is uncertain. Please revise this part again.

LITERATURE REVIEW SECTION (Chapter 2)

This research has done so many measurements to study the properties of fabricated fibrous scaffolds that also company with reference papers and citations. Personally, this research shows nice results and experimental data that match the standard and requirements of the Material department. However, the developed fibrous scaffold is going to be utilised for medical applications near future, so it is encouraged to cite and address more reference papers about further application. can broaden the topic in the literature review. Not only focus on the application of biopolymer, PVA. Following is the suggested topic that you can add to the literature review.

1. Since the context mentioned that applying the fabricated core-shell fibre mats for drug delivery application, it is suggested that a section to introduce drug delivery for wound healing application could be indicated in this part.
2. Please includes a section related to the antiseptic chlorhexidine (CHX) drug. There is a variety of drugs that could be integrated with the spinning solution. Please address the reason why this drug was selected and why it is crucial to wound healing. A table to indicate the comparison of drugs for wound healing applications could be valuable revealing in the section.
3. The core-shell fibre composite in form of a patterned scaffold was fabricated, but there are no sufficient literature reviews on the patterned scaffold. It is suggested to briefly introduce the patterned fibre mats into the study. Moreover, please also describe the importance of patterned fibre mats in drug delivery applications with some citations. Importantly, it is strongly encouraging to mention the advantages of the pattern nanofibers compared with nonwoven or aligned nanofibers in the drug delivery system.
4. On page 24, 1st paragraph, the name of the researcher/the research group could be mentioned instead of using the term “author/ reference group” for the statements describing their work.
5. Is it 330 ± 0.14 nm or it should be 330 ± 140 nm on page 24, 1st paragraph?
6. On page 26, 2nd paragraph and reference format: [8,12,40,59,60], sometimes the citation format is in form of [6], [8,21], [20]. Please recheck all citation formats and standardised them.

EXPERIMENTAL SECTION (Chapter 3):

There are some problems with writing formats. For example, on page 49, s or sec, ml or mL, and multiplication sign “x” exists as an obvious mistake (page 54). On page 50, the spacing between the text and subsection should be the same. Please check the writing spaces between the number and units carefully and revise them. On the other hand, it is strongly suggested that the number of samples (n) for each experiment must be addressed.

1. Please add the scale bar to the photo of electrospinning in Figure 1.
2. Please cite or indicate the parameters applied for making rubber mats on pages 44-45, although this technique is quite mature. (More details or why choose these parameters for making fibre mats).
3. Figures 1 and 2 are similar and repeating and could be reorganized if possible.
4. Section 3.2 (Fabrication Techniques of Core-Shell Fibers) provides prepared solutions in Table 3 and please supply a list to indicate how many and what types of fibre mates are fabricated in this thesis. Also, please name fabricated mats and address them on pages 46 or 47 (Cannot clearly realize how many samples were fabricated in section 3.2 and studied in chapter 4). For example, the samples, such as pristine PVA Fibers, Core Fibers, PVA-PEG-Si O_2, PVA-PEG-Si O_2@PVA-GO, were tested in chapter 4.
5. Please cite reference papers from the cooperated laboratory for supporting fabrication details to the 3.2.3 Patternation of fibre mats.
6. Please give the sample names of mates characterised in section 3.2.7 (Fibre mat characterization), otherwise it is quite confusing to readers in chapter 4.
7. Please add details about how you prepared samples for the characterisation and please address the names of the tested samples in section 3.2.7 (Fibre mat characterization).
8. Please mentioned which samples and how many samples were tested in the 3.2.7.1 section (Contact angle measurements). As we know, the wettability (contact angle) responds to physical and chemical properties, please clarify the features, such as density of fibre mesh, fibre diameters, surface conditions and modification, etc. in this section. Please create a structure linking this experiment and the results revealed in the next chapter.
9. On page 50, the morphology of fabricated fibbers is characterized by using observation tools, such as SEM and TEM, and the obtained averaging numbers are generally based on statistical methods and evaluations. So, I suggest addressing the sample numbers examined.
10. Pages 51 to 54 would like to study the materials properties of fabricated fibbers via using Raman spectroscopy, XRD, DSC, UV-Vis, and Tensile Stage-SEM. However, there is no obvious connection between the results measured from each piece of equipment, and maybe combine some measurements and rearrange in this chapter.

RESULTS (Chapter 4):

I strongly suggest giving a relationship and linking between measured and characterized results of tested samples. Otherwise, readers could only obtain the quantality numbers from this thesis but could not learn any physical and chemical fundamental knowledge and theory from this research.

1. Please give a brief concussion or discussion about the relationship between the measured viscosity and other results, such as mechanical properties. For example, also, is there any trend or response relative to the added amounts of GO or SiO_2, etc.?
2. On page 57 in the 1st paragraph, the candidate stated that 14 cm collection distance is the optimal parameter to form bead-free fibre and homogenous fibre coatings. However, from figure S1, the collection distance of 17 cm shows a more uniform fibre distribution than 14 cm.

It also has a lower mean diameter and standard deviation than others. The candidate can elaborate on more details by choosing 14 cm as the optimal parameter. The candidate could supplement an SEM image of nanofibers collected at 14, 17 and 21 cm for better understanding.

3. Please attaches the detected angles for sample scanning, for example, top view or tilted. Normally, the used SEM images in Fig. 4, 5, and 6 must be under the same scale bar sizes for comparison (different sizes are acceptable). Is there any link between the diameters and distributions of the fabricated fibbers and solution concentrations or weight percentages of used solutions and nanoparticles? On page 60 in Figure 4(a) and (d), the SEM images of nanofibers are vague. If have enough time, please replace it with a clear photo for a better illustration.
4. If possible, please use two different patterned collectors to fabricate the core-shell fibre composite on page 64 2nd paragraph. Which patterned fibre mats have the potential for drug delivery application? During the drug delivery experiment, which patterned fibre mats you used? Moreover, it states that the topography of fibre mats is a crucial factor in the case of cell adhesion. If possible, it is suggesting conducting a cell cytotoxicity test (at least 3 days) to determine whether the fabricated fibre mats have the potential to exhibit cell growth. The cell cytotoxicity test also could confirm that there is no adverse effect of using graphene oxide in your study.
5. It is confusing whether the patterned fibre mats were used throughout the study or not. In Figure 7, the experiment looks like using a nonwoven fibre mat and it is not matched to the patterned fibre mats. By the way, the indicator of the yellow arrow in Figure 7 and the blue arrow in Figure 8 could be included in the figure caption.
6. The effect of water uptake was studied and revealed in Figure 7. Unfortunately, readers normally are keen to know the water uptake responses to the time independence. The purpose of this research might be to develop a highly potential fibre scaffold for bio and medical applications in near future. Therefore, testing the water absorbance ratios and speeds of fibrous scaffolds under the high moisture environment or attached to wet substrates.
7. Please provide some reference papers to support the short concussion mentioned “where PEG functions as a good dispergator” on page 69. Normally, we use more mixture ratios or over 3 mixtures samples to show the effect and behaviours (it is incomprehensive, although you show the results in Fig 9(c)).
8. Please address sample number (n=?) tested in section 4.5 (Contact angle and Fibre Diameter) and Fig 9.
9. In section 4.6 (Raman Spectroscopy) and 4.7 (FTIR spectroscopy) were applied to study the fabricated fibbers please have a connection relative with the surface conditions of SEM images or TEM images, if possible (maybe could add some images in the SEM result section) and address relationships between each peak (bandwidth) and fibre surface details.
10. It is very nice to apply the ToF-SIMS to study drug loading but unfortunately there are not enough comments and conclusions addressed on page 80.

11. Maybe could combine sections 4.9 (XRD) and 4.10 (DSC), and not too many details mentioned the sample preparation and numbers.
12. Mechanical testing section does not provide enough tastings to different parameters of samples and as well-known that the mechanical properties are likely following the fibre numbers (thickness and density) and orientation of fibbers in the tested mats.

CONCLUDING REMARKS (Chapter 5):

I am personally aware that there are no strong viewpoints categorized from your research funding and the summary conclusions on page 105 could not clearly deliver significate contributions discovered from all experimental studying to readers, after reading the conclusion part. I recommend that please rearrange and remodify this chapter.

1. I personally suggest that the explanations from pages 102 to 104 and illustration figure 25 could be reorganized and rearranged to chapter 4 or other sections. The discussions and explanations are normally provided in the results and discussion section.

SUPPLEMENTARY MATERIALS (From page 106):

1. If possible, please replace it with a better SEM-Image for Figure S4 on page 110. Please mentioned what the dimension is for the pattern on the Si wafer and how the patterned fibre mats are revealed after peeling. These details could be included in the result section.

Bibliography

There are some problems with the reference format. Please recheck whether the format of the references required a full name of the journal or using the abbreviation, words such as Vol., page, should be inserted or not, and please revise them. Examples as shown below.

1. Pisani, S.; Genta, I.; Tiziana Modena, ·; Dorati, R.; Bruni, G.; Benazzo, M.; Conti, B. A Proof of Concept to Define the Parameters Affecting Poly-l-Lactide-Co-Poly-ε-Caprolactone Shape Memory Electrospun Nanofibers for Biomedical Applications. *Drug Delivery and Translational Research 2022* **2022**, 1–15, doi:10.1007/S13346-022-01218-2.

3. Wu, J.; Xie, L.; Lin, W.Z.Y.; Chen, Q. Biomimetic Nanofibrous Scaffolds for Neural Tissue Engineering and Drug Development. *Drug Discov Today* **2017**, *22*, 1375–1384, doi:10.1016/j.drudis.2017.03.007.

59. Li, H.; Chen, X.; Lu, W.; Wang, J.; Xu, Y.; Guo, Y. Application of Electrospinning in Antibacterial Field. *Nanomaterials 2021, Vol. 11, Page 1822* **2021**, *11*, 1822, doi:10.3390/NANO11071822.

61. Liu, P.; Chen, W.; Liu, C.; Tian, M.; Liu, P. A Novel Poly (Vinyl Alcohol)/Poly (Ethylene Glycol) Scaffold for Tissue Engineering with a Unique Bimodal Open-Celled Structure Fabricated Using Supercritical Fluid Foaming. *Sci Rep* **2019***, 9*, 1–12, doi:10.1038/s41598-019-46061-7.

172. Simon, M.A.; Anggraeni, E.; Soetaredjo, F.E.; Santoso, S.P.; Irawaty, W.; Thanh, T.C.; Hartono, S.B.; Yuliana, M.; Ismadji, S. Hydrothermal Synthesize of HF-Free MIL-100(Fe) for Isoniazid-Drug Delivery. Scientific Reports *2019 9:1* **2019***, 9*, 1–11, doi:10.1038/s41598-019-53436-3.

Comment to candidate

In this work, the candidate fabricated core-shell fibbers composite or biomedical applications by using the coaxial electrospinning technique. Several experiments were designed to characterize the fabricated core-shell fibre mats and plentiful and massive quantified data were measured and presented. Also, the candidate has published her results in several nice academic journals under professional reviewers from all over the world, so I do not have too much concern about the data and results done by you. However, there's plenty of room at the bottom and I would like to encourage the candidate to address more connections between each measured result accomplished with fundamentals and theories. Then, readers could learn from your academic contributions and discoveries. Otherwise, after reading it, I only obtained and learned about so much data that you measured and so many tools you utilized and only presented in this thesis. Moreover, all presented data must be accurate and precise because of a standard required by an academic manuscript so please carefully recheck all data in the whole thesis again. Finally, your contributions are based on the time, effort, and energy to which you donated, and all have been concluded in this thesis. Hope you are satisfied and achieving successful work during your Ph.D. studying period.