RGC Ref. No.:
UGC/FDS11/P01/21
(please insert ref. above)

RESEARCH GRANTS COUNCIL
COMPETITIVE RESEARCH FUNDING SCHEMES FOR THE LOCAL SELF-FINANCING DEGREE SECTOR

FACULTY DEVELOPMENT SCHEME (FDS)

Completion Report
(for completed projects only)

Submission Deadlines:	1. *Auditor's report with unspent balance, if any: within **six** months of the approved project completion date.* 2. *Completion report: within **12** months of the approved project completion date.*

Part A: The Project and Investigator(s)

1. Project Title

Key fundamental issues about the preparation of multiple-layer Janus functional nanofibers through electrospinning

2. Investigator(s) and Academic Department(s) / Unit(s) Involved

Research Team	**Name / Post**	**Unit / Department / Institution**
Principal Investigator	Prof BLIGH Annie Sim-wan / Provost	Office of President and School of Health Sciences / Caritas Institute of Higher Education
Co-Investigator(s)	Prof YU Dengguang / Team Leader	School of Materials Science and Engineering / University of Shanghai for Science and Technology

3. Project Duration

	Original	**Revised**	**Date of RGC / Institution Approval** *(must be quoted)*
Project Start Date	01/01/2022	N/A	N/A
Project Completion Date	31/12/2023	30/06/2024	27/11/2024
Duration *(in month)*	24	30	27/11/2024
Deadline for Submission of Completion Report	31/12/2024	30/06/2025	27/11/2024

4.4 Please attach photo(s) of acknowledgement of RGC-funded facilities / equipment.
N/A

Part B: The Final Report

5. Project Objectives

5.1 Objectives as per original application

1. to develop 3-fluid side-by-side electrospinning (including traditional one and the modified one), and to build a series of controllable methods for creating 3-layer Janus nanostructures. Among all kinds of tri-fluid processes, 3-fluid side-by-side electrospinning is the most difficult one due to the repulsion of working fluids with the same charges.
2. to elaborate the nanofabrication mechanism through understanding the interfacial interactions between different working fluids on the multiple-fluid electrospinning processes and the quality of the final nanoproducts. Clarifying the fluid behavior characteristics under high voltage electrostatic field and the formation mechanism of the 3-layer Janus nanostructure
3. to produce tri-layer side by side nanofibers suitable for loading chemical molecules (such as drug like molecules) for the elucidation of the nanofiber-based structure-performance relationships

5.2 Revised objectives

Date of approval from the RGC: N/A

Reasons for the change: N/A

1.

2.

3. ....

5.3 Realisation of the objectives
(Maximum 1 page; please state how and to what extent the project objectives have been achieved; give reasons for under-achievements and outline attempts to overcome problems, if any)

Objective 1
To develop 3-fluid side-by-side electrospinning (including traditional one and the modified one), and to build a series of controllable methods for creating 3-layer Janus nanostructures. Among all kinds of tri-fluid processes, 3-fluid side-by-side electrospinning is the most difficult one due to the repulsion of working fluids with the same charges.

We have completed the development of both traditional and modified 3-fluid side-by-side electrospinning processes for constructing 3-layer nanostructures. Factors such as working fluids, applied voltage, spinnable and non-spinnable working fluids, design of spinneret and flow rate were successfully optimized for creating desired tri-layers nanofibers. The data were published, **J1**: DOI: 10.3390/pharmaceutics.2022.14061208; **J2**: DOI: doi.org/10.1016/j.apmt.2023.101766; and presented **C1** – **C3**.

Objective 2
To elaborate the nanofabrication mechanism through understanding the interfacial interactions between different working fluids on the multiple-fluid electrospinning processes and the quality of the final nanoproducts. Clarifying the fluid behavior characteristics under high voltage electrostatic field and the formation mechanism of the 3-layer Janus nanostructure

In this project we have elaborated the nanofabrication mechanism and clarified the fluid behaviour characteristics under high voltage electrostatic field and the formation mechanism of the 3-layer Janus nanostructure. The results are presented in a paper published in Materials and Design, **J3**: DOI: 10.1016/j.matdes.2023.111652. In tri-fluid side-by-side electrospinning, three sections with different ratios of polymers were integrated into one microfiber. Thus, forming a clear boundary from an overhead view is difficult, as different sections overlap. In the same work under electric field force, which is generated by a high-voltage electrostatic generator (ZGF-60 kV/2 mA) the working fluid was ejected from the Taylor cone formed at the tip of the spinneret when electrostatic repulsion had exceeded the interaction among working solutions and a straight jet was followed by. The working fluid would experience bending and swing stage to stretch working fluid into nano/micro scale.

Objective 3
To produce tri-layer side by side nanofibers suitable for loading chemical molecules (such as drug like molecules) for the elucidation of the nanofiber-based structure-performance relationships

A review entitled “A Review on Electrospun Poly (amino acid) Nanofibers and Their Applications of Hemostasis and Wound Healing” was completed and published (R1: Biomolecules, 2022, 12(6): 794) during the project period. The review covers the study of single fluid, double fluid and multifluid nanofibers as functional nanofibers in wound dressing.

Functional nanofibers with potential medical applications were developed and characterised. Optimized medicated 3-layer side by side nanofibers with known characteristics (from objective 2) as a proof of concept of potential functional nanofibers in medicine. They were evaluated for their potential applications such as drug delivery systems (**J4**, DOI: 10.1016/j.ijpharm.2024.124180) and wound dressing (**J5**, DOI: 10.3390/nano14070646; **J6,** CEJ 2024 accepted). We have developed a new side-by-side electrospinning process, ie a co-shell solvent was used to prevent the separation of two side-by-side working fluids during the nanofabrication process, creating medicated nanofibers with enhanced icariin delivery efficiency (**J4**). In **J6** a proof-of-concept study on the fabrication and functionalization of electrospun complex nanostructures and the study successfully addressed the issue of tissue adhesion impeding the healing process of injured tendons.

5.4 Summary of objectives addressed to date

Objectives *(as per 5.1/5.2 above)*	**Addressed** *(please tick)*	**Percentage Achieved** *(please estimate)*
1. to develop 3-fluid side-by-side electrospinning (including traditional one and the modified one), and to build a series of controllable methods for creating 3-layer Janus nanostructures. Among all kinds of tri-fluid processes, 3-fluid side-by-side electrospinning is the most difficult one due to the repulsion of working fluids with the same charges	✓	100%
2. to elaborate the nanofabrication mechanism through understanding the interfacial interactions between different working fluids on the multiple-fluid electrospinning processes and the quality of the final nanoproducts	✓	100%
3. to produce tri-layer side by side nanofibers suitable for loading chemical molecules (such as drug like molecules) for the elucidation of the nanofiber-based structure-performance relationships	✓	100%

6. Research Outcome

6.1 Major findings and research outcome
(Maximum 1 page; please make reference to Part C where necessary)

Here is a summary of the major findings and research outcomes from the objectives presented:

a. Developed successfully with reproducibility of both traditional and modified 3-fluid side-by-side electrospinning processes to create 3-layer Janus nanostructures.
b. Optimized factors like working fluids, applied voltage, spinnable/non-spinnable fluids, spinneret design, and flow rates enabling the production of desired tri-layer nanofibers.
The research findings were published in papers J1, J2, and presented in conferences C1-C3.
c. Elaborated the nanofabrication mechanism by understanding the interfacial interactions between the working fluids and the fluid behavior characteristics under the high voltage electrostatic field. The results facilitated the understanding of structural architecture in creating nanofibers of specific performances.
d. Clarified the formation mechanism of the 3-layer Janus nanostructure. *The results were published in paper J3*.
e. Produced tri-layer side-by-side nanofibers suitable for loading chemical/drug molecules. Although successful fabrication in this area was made, we need to study more on loading capability of working solutions and delivery performances. In *J5,* we have demonstrated simultaneous loading of multiple active ingredients could impart specific nanofibers with diverse functional performances, further expanding their potential applications in wound management, for example.
f. Developed optimized medicated 3-layer side-by-side nanofibers and elucidated the nanofiber-based structure-performance relationships for drug delivery (*J4*) and wound dressing (*J6*) applications.

Overall, the research successfully developed novel 3-layer Janus nanostructures, elucidated the nanofabrication mechanisms, and produced functional nanofibers with potential biomedical applications.

6.2 Potential for further development of the research and the proposed course of action *(Maximum half a page)*

Here are some possible future directions and courses of action:

a. We can explore incorporating a wider range of polymers, drugs, and other functional components into the 3-layer nanofibers. This could lead to the development of more sophisticated and tailored nanostructures for diverse applications.
b. Building on the current understanding of the nanofabrication mechanisms, we can further optimize the structure, composition, and properties of the 3-layer nanofibers to enhance their performance as drug delivery systems, wound dressings, and other biomedical materials.
c. Developing strategies to scale up the 3-fluid electrospinning process would enable the transition from lab-scale demonstrations to pilot-scale or industrial-scale manufacturing. This could involve designing specialized multi-spinneret setups or investigating alternative high-throughput electrospinning techniques.
d. The versatile 3-layer Janus nanofibers could be investigated for other potential applications beyond biomedical uses, such as in areas like energy storage, filtration, or composite materials.

7. Layman's Summary

(Describe in layman's language the nature, significance and value of the research project, in no more than 200 words)

This research project focused on developing a novel 3-layer nanofiber structure called "Janus nanostructures" using an advanced electrospinning technique. Electrospinning is a method to produce ultra-fine fibers with diameters in the nanometer range.

The key significance of this work is that it successfully created a complex 3-layer nanofiber structure, which is challenging to achieve. We have optimized various factors like the liquids used, voltages applied, and the spinneret design to produce these intricate nanofibers.

The significance of this research lies in the potential applications of these 3-layer nanofibers. We have demonstrated that these nanofibers can be used to carry and deliver drugs for biomedical function. We also showed that the nanofibers have properties that could make them useful for wound dressing applications, helping injured tissues heal better.

Overall, this project advanced the fundamental understanding of complex nanofiber fabrication and opened up new opportunities to develop innovative nanomaterials for biomedical and healthcare applications. The findings have been widely published in peer-reviewed journals, showcasing the scientific impact of this research.

Part C: Research Output

8. Peer-Reviewed Journal Publication(s) Arising Directly From This Research Project

(Please attach a copy of the publication and/or the letter of acceptance if not yet submitted in the previous progress report(s). All listed publications must acknowledge RGC's funding support by quoting the specific grant reference.)

The Latest Status of Publications				Author(s) *(denote the correspond-ing author with an asterisk*)*	Title and Journal / Book *(with the volume, pages and other necessary publishing details specified)*	Submitted to RGC *(indicate the year ending of the relevant progress report)*	Attached to this Report *(Yes or No)*	Acknowledged the Support of RGC *(Yes or No)*	Accessible from the Institutional Repository *(Yes or No)*
Year of Publication	Year of Acceptance *(For paper accepted but not yet published)*	Under Review	Under Preparation *(optional)*						
2022				Menglong Wang, Deng-Guang Yu*, Gareth R Williams, Sim Wan Annie Bligh*	Co-Loading of Inorganic Nanoparticles and Natural Oil in the Electrospun Janus Nanofibers for a Synergetic Antibacterial Effect[J]. Pharmaceutics, 2022, 14(6): 1208.	J1 (2022)	*No*	*Yes*	*Yes*
2022				Yuexin Ji, Wenliang Song, Lin Xu, Deng-Guang Yu*, Sim Wan Annie Bligh*	A Review on Electrospun Poly (amino acid) Nanofibers and Their Applications of Hemostasis and Wound Healing[J]. Biomolecules, 2022, 12(6): 794.	R1 (2022)	*No*	*Yes*	*Yes*
2023				Menglong Wang, Deng-Guang Yu*, Sim Wan Annie Bligh*	Progress in preparing electrospun Janus fibers and their applications, Applied Materials Today, 2023, 31, 101766.	J2 (2023)	*Yes*	*Yes*	*Yes*
2023				Menglong Wang, Deng-Guang Yu*, Gareth R Williams, Sim Wan Annie	Exploring wettability difference-driven wetting by utilizing electrospun chimeric Janus microfiber comprising	J3 (2023)	*Yes*	*Yes*	*Yes*

				Bligh*	**cellulose acetate and polyvinylpyrrolidone, Materials & Design, 2023, 226, 111652.**				
2024				**Y. Sun, J. Zhou, Z. Zhang, Deng-Guang Yu*, Sim Wan Annie Bligh***	**Integrated Janus Nanofibers Enabled by A Co-Shell solvent for Enhancing Icariin Delivery Efficiency, Intl. J. Pharmaceutics, 2024, 658, 124180.**	**J4 (2024)**	***Yes***	***Yes***	***Yes***
2024				**Chang Huang, Menglong Wang, Deng-Guang Yu*, Sim Wan Annie Bligh***	**Electrospun Fenoprofen/Polycaprolactone @ Tranexamic Acid/Hydroxyapatite Nanofibers as Orthopedic Hemostasis Dressings, Nanomaterials 2024, 14(7), 646**	**J5 (2024)**	***Yes***	***Yes***	***Yes***
2024				**Lin Xu, Qisheng Li, Haibing Wang, Hui Liu, Deng-Guang Yu*, Sim-Wan Annie Bligh*, Xuhua Lu***	**Electrospun Multi-functional Medicated Tri-Section Janus Nanofibers for An Improved Anti-Adhesion Tendon Repair, Chemical Engineering Journal 2024, 492, 152359**	**J6 (2024)**	***Yes***	***Yes***	***Yes***

9. Recognized International Conference(s) In Which Paper(s) Related To This Research Project Was / Were Delivered

(Please attach a copy of each conference abstract)

Month / Year / Place	**Title**	**Conference Name**	**Submitted to RGC** *(indicate the year ending of the relevant progress report)*	**Attached to this Report** *(Yes or No)*	**Acknowledged the Support of RGC** *(Yes or No)*	**Accessible from the Institutional Repository** *(Yes or No)*
Sept/2023/Italy	Keynote Talk: Key issues of multifluid side-by-side electrospun tri-layer Janus fiber	6th International Conference on Materials Science & Nanotechnology	C1 (2023)	***Yes***	***Yes***	***No***

Sept/2023	Poster: Multifluid side-by-side electrospun tri-layer Janus fiber with different spinnable solutions	IEEE-NAP-2023 Nanomaterials: Applications & Properties doi: 10.1109/NAP59739.2023.10310796	C2 (2023)	***Yes***	***Yes***	***No***
Sept/2023	Short Talk: Oral side-by-side electrospun PCL-Ag NPs/CA-Lavender oil Janus nanobelt as a potential dressing	IEEE-NAP-2023 Nanomaterials: Applications & Properties doi: 10.1109/NAP59739.2023.10310821.	C3 (2023)	***Yes***	***Yes***	***No***

10. Whether Research Experience And New Knowledge Has Been Transferred / Has Contributed To Teaching And Learning
(Please elaborate)

The research experience is shared with undergraduate and master project students interested in biomaterials research.

11. Student(s) Trained
(Please attach a copy of the title page of the thesis)

Name	Degree Registered for	Date of Registration	Date of Thesis Submission / Graduation
N/A			

12. Other Impact
(e.g. award of patents or prizes, collaboration with other research institutions, technology transfer, teaching enhancement, etc.)

We managed to collaborate with a number of clinical establishments in China, for example, Department of Outpatient, Third Affiliated Hospital of Navy Military Medical University, Shanghai 200438, China; Department of Neurosurgery, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai; 200025, China; and Department of Orthopaedics, Shanghai Changzheng Hospital, Naval Medical 10 University, Shanghai 200001, China. We also collaborate with one research institution, ie UCL School of Pharmacy, University College London, London, WC1E 6BT, UK

13. Statistics on Research Outputs

	Peer-reviewed Journal Publications	Conference Papers	Scholarly Books, Monographs and Chapters	Patents Awarded	Other Research Outputs (please specify)	
No. of outputs arising directly from this research project	6	3			Type	No.

14. Public Access Of Completion Report

(Please specify the information, if any, that cannot be provided for public access and give the reasons.)

Information that Cannot Be Provided for Public Access	Reasons
N/A	