RGC Ref. No.: UGC/FDS16/M08/18
(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

Radial Basis Functions Method for Medical Imaging Problems

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

Research Team	Name / Post	Unit / Department / Institution
Principal Investigator	CHAN Moon-tong / Assistant Professor	Department of Electronic Engineering and Computer Science / Hong Kong Metropolitan University
Co-Investigator(s)	N.A.	N.A.
Others	N.A.	N.A.

3. Project Duration

	Original	Revised	Date of RGC / Institution Approval *(must be quoted)*
Project Start Date	1/January/2019	N.A.	
Project Completion Date	31/December/2020	30/June/2022	5/May/2021
Duration *(in month)*	24	42	5/May/2021
Deadline for Submission of Completion Report	31/December/2021	31/December/2022	5/May/2021

Part B: The Final Report

5. Project Objectives

5.1 Objectives as per original application

1. To investigate theories and mathematical models of medical image reconstruction problems from different image modalities, such as computed tomography and magnetic resonance imaging.
2. To develop a meshless computational method for numerical approximation to the solution of the model on image reconstruction selected in (1).
3. To implement the developed computational method obtained in (2) for practical use in radiotherapy treatment planning.

5.2 Revised objectives

Date of approval from the RGC:	N.A.
Reasons for the change:	N.A.

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)

As for Objective 1, we have fully realized the objective stated.

(i) First Published Journal Article (Please refer to Part C-8)
We have investigated various theories about binding affinity prediction (BAP) using complex protein-ligand complex structures. We then adopted a building-block-based taxonomy to review a wide range of protein-ligand interaction fingerprints (IFPs) models and compared representative IFP-based machine learning scoring functions (SFs) in target-specific and generic scoring tasks.

(ii) Second Published Journal Article (Please refer to Part C-8)
To efficiently achieve putative protein-ligand complexes for BAP problems, we have integrated structural descriptors and machine-learning models by introducing the profiles of intermolecular contacts (IMCPs) as descriptors for machine-learning-based BAP. IMCPs are employed to describe each group of protein-ligand contacts by the count and average distance of the group members and collaborate closely with classical machine-learning models.

As for Objective 2, we have fully realized the objective stated.

Third Published Journal Article (Please refer to Part C-8)
For the distance map obtained by distance transformation as the learning weight of the region of interest (ROI) edge of medical images, a new segmentation framework based on two-stage learning have been proposed specifically to (1) use a simple two-stage network as the basic network framework and design a branch in its first stage to incorporate distance map information, (2) design and discuss three methods for generating distance maps with edges as the target to effectively express the weights used to guide deep learning, and (3) further optimize network learning, Distdice Loss is proposed to emphasize the contribution of distance map to network training.

As for Objective 3, we have fully realized the objective stated.

Fourth Published Journal Article (Please refer to Part C-8)
We have developed a new network for learning video-level classification of breast lesions. Additionally, we have proposed a contrastive learning–guided multi-meta attention network (CLMAN) by combining both a deformed feature extraction module and a multi-meta attention module to deal with breast lesion diagnosis in ultrasound breast sequence in arbitrary length.

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 investigate theories and mathematical models of medical image reconstruction problems from different image modalities, such as computed tomography and magnetic resonance imaging.	✓	100%
2. To develop a meshless computational method for numerical approximation to the solution of the model on image reconstruction selected in (1).	✓	100%
3. To implement the developed computational method obtained in (2) for practical use in radiotherapy treatment planning.	✓	100%

6. Research Outcome

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

First Journal Article
Binding affinity prediction is essential for computer-aided drug design. In comparison with the representative IFP scores of various IFP-based SFs using multiple datasets for validation, atom-pair-counts-based and substructure-based IFPs are found to demonstrate great potential in target-specific and generic scoring tasks for machine-learning based binding affinity prediction problems. The research outcome has been presented and published in the first journal article in Part C-8.

Second Journal Article
We have expanded intermolecular contacts (IMCs) to IMC profiles (IMCPs) by taking into consideration the average distance for every sort of IMCs that improves the BAP accuracy but maintains the simplicity and model interpretability of the descriptors. With training and validation by multiple datasets, we find that IMCP-based models often lead to better BAP accuracy than those models originating from other similar descriptors for structure-based drug design and that IMCPs are simple, concise, and easy to interpret in model training. In addition, our study suggests that IMCP descriptors can greatly conclude the structural information of protein-ligand complexes and that they can be easily updated with personalized profile features. We have implemented the IMCPs in the BAP Toolkit on github (https://github.com/debbydan-wang/BAP). The research outcomes have been presented and published in the second journal article in Part C-8.

Third Journal Article
The Dice score and Assd of the method we constructed on the ASC dataset are improved in comparison with the two-stage network. The training is divided into two stages. In the first stage, two branches are derived to predict the rough segmentation of the left atrium and the distance map, respectively, and the two are merged into the second stage of training to obtain accurate segmentation results. Experimental results indicate that our network sets a new state-of-the-art performance on the left atrium MRI segmentation dataset. The research outcome has been presented and published in the third journal article in Part C-8.

Fourth Journal Article
Four research outcomes are achieved in this research. First, we have developed a new network for learning video-level classification of breast lesions. Second, we have collected an ultrasound video dataset consisting of 268 sequences for breast lesion classification. Third, the proposed feature extraction module can autonomously and adaptively obtain essential information of the feature map in the spatial dimension, whereas the designed multi-meta attention module can gather effective information in the temporal dimension. Moreover, we have employed a contrast learning strategy to reduce the high imaging variability problem within ultrasound lesion videos. Last, experimental results based on the collected video dataset reflect that the proposed CLMAN considerably outperforms the state-of-the-art methods for video classification. The research outcomes have been presented and published in the fourth journal article in Part C-8.

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

The research outcomes of this project could be applied to binding affinity prediction, detection of location of organ lesions and medical image diagnosis. For binding affinity prediction, our reviews of different IFP models and comparison of IFP-based scoring functions could give insights for computer-aided drug design. Future research could focus on dealing with (1) fluctuations resulted from altering model types and parameters, and (2) more and qualified data to promote the development of machine-learning scoring functions further. For lesion segmentation, our proposed method of distance transformation can handle the partial volume effect of organ tissues, that is, the unclear and blurred edges of ROI in medical images. In the future, research can be done to cover all three loss functions for joint training and exploring space of optimization models to extend the scope of applications. For medical image diagnosis, our proposed automatic diagnosis model for ultrasound sequences can achieve significantly higher accuracy in classification recognition to assist medical diagnosis tasks using deep learning methods compared with other existing sophisticated classification methods. The future research direction would be on the adaptation of the current approach to achieve higher evaluation metric values for better module performance.

7. Layman's Summary

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

The protein-ligand interaction fingerprints (IFPs) for binding affinity prediction (BAP) are essential to computer-aided drug design. IFPs are competitive because of their simple representations, elaborate profiles of key interactions and easy collaborations with machine-learning algorithms. For structure-based drug design, the profiles of intermolecular contacts (IMCPs) as descriptors are simple, concise and interpretable. These descriptors greatly conclude the structural information of protein-ligand complexes and can be easily updated with personalized profile features.

The lesion segmentation framework based on distance transformation can assist in medical image diagnosis. It has the merit of handling unclear and blurred tissue edges for region of interest in medical images with high-accuracy segmentation of lesions or organs.

The guided multi-meta attention network (CLMAN) is an automatic ultrasound imaging diagnosis method. It is also a non-invasive, inexpensive, safe, and free of ionizing radiation method that can achieve significantly higher accuracy in classification recognition to assist medical diagnosis tasks compared with other advanced methods. Such a computer-aided diagnosis can handle low-quality imaging and reduce the workload of radiologists. Consequently, the operation-dependent impact of ultrasound imaging can be minimized.

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 corresponding 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)*						
2021				Debby Dan Wang*, Moon-Tong Chan; Hong Yan	Structure-based protein–ligand interaction fingerprints for binding affinity prediction. *Computational and Structural Biotechnology Journal*, *19*, 6291-6300.	No	Yes (Attachment 1)	Yes	Yes
2021				Huang, X., Lin, Z., Jiao, Y., Chan, M. T., Huang, S*., & Wang, L. (2021).	Two-Stage Segmentation Framework Based on Distance Transformation. *Sensors*, *22*(1), 250.	No	Yes (Attachment 2)	No#	Yes
2022				Debby Dan Wang*, Moon-Tong Chan	Protein-ligand binding affinity prediction based on profiles of intermolecular contacts. *Computational and Structural Biotechnology Journal*, 20, 1088-1096.	No	Yes (Attachment 3)	Yes	Yes
2022				Huang, X., Lin, Z., Huang, S., Wang, F. L., Chan, M. T.*, & Wang, L.	Contrastive learning–guided multi-meta attention network for breast ultrasound video diagnosis. *Frontiers in Oncology*, *12*.	No	Yes (Attachment 4)	Yes	Yes

Being occupied with meetings, administrative work and heavy teaching load during the period of preparing, submitting and revising the article, the authors accidentally left out the acknowledgement of the research fund from RGC. The article was published in Dec 2021 and the journal notified the authors in Dec 2022 about a formal publication. Thus, we cannot add back the acknowledgement.

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)*
N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.

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

The research experience has contributed to the PI's learning and teaching in data science related courses (e.g., final year project: Data Science Project). It widens the PI's horizons and enriches his knowledge in the field. Moreover, the research experience gained from and research methodology employed in the project inspire some final year project topics relevant medical image diagnosis.

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**
Nil			

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

Nil

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	4	0	0	0	Type: N.A.	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
Nil	