Guest Editorial Computational Mathematics Modeling in Cancer Analysis

CANCER is a complex disease that can affect any body part. One key feature of cancer is the rapid production of abnormal cells that grow beyond their usual borders and can invade adjoining parts of the body and spread/metastasized to other organs. The process of metastasis is the crucial cause of cancer death. Environmental factors are a significant contributor to cancer initiation [1]. Numerous studies investigate various aspects of cancer, including pathogenesis, prevention, diagnosis, and treatment methods, with the goal of improving patient quality of life and increasing survival rates. Despite significant advances in the field, cancer continues to represent a global challenge for prevention and treatment.

Over the past few decades, many mathematical methods have been applied to cancer research, assisting physicians and scientists in basic cancer classification and predictive diagnosis, among many other applications. Advanced computational methods for cancer data analysis, motivated by rigorous mathematical theory and biological mechanisms, are robust and clinically useful. Computational Mathematics Modelling (CMM) is the process of applying mathematical methods and computer techniques to the solution of real-world problems. It combines both mathematical modelling and computer simulation and aims to describe and analysis real systems with complexity and uncertainty. By constructing mathematical models, researchers can simulate cancer cell proliferation, spread and treatment responses and reveal cancer development's laws and characteristics. Understanding the complex nature of cancer will help clinicians make more informed decisions. This enhances decision-making support ultimately leads to improved treatment outcomes and higher patient survival rates.

With the advancement of available medical testing technologies, we are able to access multimodal cancer data including, but not limited to, radiology, pathology, genomics and proteomics. There are still many challenges in considering and truly exploiting complex multimodal data for the selection of precision cancer diagnosis and treatment options. Therefore, advanced computational mathematical modelling techniques are needed to extract more meaningful information from the complex and growing body of cancer data to help diagnose and treat cancer.

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Artificial intelligence (AI) and machine learning have significantly influenced many facets of the healthcare sector. Advancement in technology has paved the way for analysis of big datasets in a cost- and time-effective manner. Clinical oncology and research are reaping the benefits of AI [2]. There are already a number of research studies suggesting that AI can perform as well as or better than humans at key healthcare tasks, such as diagnosing disease [3].

In addition, research on the mathematical theory of interpretability in cancer imaging analysis, computational modelling of tumor evolution, and topological maps for prognostic analysis has facilitated large-scale integration of cancer data analysis, providing valuable insights to academic researchers. These studies play a crucial role in facilitating professional uptake of advances in biomedical and computational pathology.

With all these in mind, this special issue focuses on major trends and challenges in theoretical, computational, and applied aspects of computational mathematics in cancer data analysis for cancer research and clinical diagnosis/therapy.

The first to fifth papers focus on tumor feature engineering in the hope of extracting more discriminative features for subsequent cancer analysis.

The first paper by Rui Yan et al. [4] considers that modeling the global context of gigapixel whole slide image (WSI) using a vanilla transformer is prone to overfitting due to less data and unable to acquire hierarchical WSI representation. To address these problems, in this paper, it proposes a novel Sparse and Hierarchical Transformer (SH-Transformer) for survival analysis. Specifically, this paper introduces sparse self-attention to alleviate the overfitting problem.

The second paper by Ziqi Zhao et al. [5] focus on tumor progression after ablation by a novel survival analysis framework for survival prediction and efficacy assessment. In the feature extraction phase, it extracts preoperative and postoperative MRI radiomics features and vision transformer-based deep learning features and combines the immune features extracted from peripheral blood immune responses using flow cytometry and routine blood tests before and after treatment. The random survival forest and improved deep Cox mixture (DCM) are applied to select features and generate predictions respectively. To better accommodate input features of different types, a self-adapting fully connected layer has been proposed. This layer enables the local and global representation of features.

The third paper by Fan Song et al. [6] takes into account the fact that current feature engineering methods are not able to fully

and effectively exploit feature heterogeneity when dealing with different types of radiomics features. For this reason, this paper proposes a novel feature engineering approach to reconstruct a set of latent space features from original shape, intensity and texture features. This proposed method projects features into a subspace called latent space, in which the latent space features are obtained by minimizing a unique hybrid loss function including a clustering-like loss and a reconstruction loss.

The fourth paper by Jiawei Zhang et al. [7] considers necessary to learn discriminative features for Isocitrate dehydrogenase (IDH) prediction. However, it is a comprehensive challenge based on highly heterogeneous of the gliomas in MRI. To address these issues, it proposes a multi-level feature exploration and fusion network (MFEFnet) to comprehensively explore discriminative IDH-related features and fuse different features at multiple levels for accurate IDH prediction in MRI. The interpretability of the different modules is also evaluated to illustrate the effectiveness and credibility of the method.

The fifth paper by Shijie Zhao et al. [8] takes into account of accurate genotyping of the epidermal growth factor receptor (EGFR). Most methods require physicians to annotate tumor boundaries and does not sufficiently exploit the multilevel features for final prediction. To solve these problems, it proposes a Denseformer framework to identify EGFR mutation status in a real end-to-end fashion directly from 3D lung CT images, which fully explores the distinctive information across the different level features.

The sixth to seventh papers deal mainly with pathological image processing, with a significant emphasis on weakly supervised segmentation tasks and cross-domain nucleus detection tasks.

The sixth paper by Yilong Li et al. [9] focus on Weakly supervised segmentation model. it presents a sketch-supervised method, called DCTGNCAM, based on a dual CNN-Transformer network and a modified global normalized class activation map. By modelling global and local tumor features simultaneously, the dual CNN-Transformer network produces accurate patch-based tumor classification probabilities by training only on lightly annotated data. In addition, it collects a private skin cancer dataset named BSS, which contains fine and coarse annotations for three types of cancer.

The seventh paper by Zhi Wang et al. [10] focus on cross-domain nuclei detection task. The small size of nuclei presents a challenge that negatively affects feature alignment. In addition, the lack of annotations in the target domain can significantly complicate the alignment process. To address these challenges, it proposes an end-to-end graph-based nuclei feature alignment (GNFA) method for boosting cross-domain nuclei detection. Nuclei graph convolutional network (NGCN) aggregating information of adjacent nuclei to generate sufficient nuclei features, and importance learning module (ILM) is designed to further select discriminative nuclei features.

The eighth paper by Hsienchih Ting et al. [11] aims to integrate the incomplete multimodal MRI data for accurate segmentation of brain tumor. Multimodal magnetic resonance imaging (MRI) can provide rich and complementary information for accurate brain tumor segmentation. However, some modalities may be absent in clinical practice. In order to better learn the features of missing modalities, the novel network is founded on the U-Net structure, comprising modality-specific encoders, a multimodal transformer and a multimodal shared-weight decoder. A missing-full complementary learning strategy is used to explore the latent correlation between the missing and full modalities for feature compensation.

The ninth to twelfth papers focus on the evaluation and application of computer-assisted diagnostic cancer modelling with detailed modelling of medical diagnosis from different perspectives.

The ninth paper by Wen Li et al. [12] sought to examine the GFCE-MRI model's generalizability by using data from seven institutions and altering the heterogeneity of training MRI information across five commonly used normalization methods. It uses Three state-of-the-art neural networks were applied to map from T1-weighted and T2-weighted MRI to contrast-enhanced MRI (CE-MRI) for GFCE-MRI synthesis in patients with nasopharyngeal carcinoma. MRI data from three institutions were used separately to generate three uni-institution models and jointly for a tri-institution model. The five normalization methods were applied to normalize the training and testing data of each model. MRI data from the remaining four institutions served as external cohorts for model generalizability assessment.

The tenth paper by Liangliang Liu et al. [13] addresses report on the impact of the high consistency of disease subtypes and uneven distribution of cancer cells on the performance of multi-classification methods. For this reason, this paper proposes a collaborative transfer network (CTransNet) for multi-classification of breast cancer histopathological images. CTransNet consists of a transfer learning backbone branch, a residual collaborative branch, and a feature fusion module. The transfer learning branch adopts the pre-trained DenseNet structure to extract image features from ImageNet.

The eleventh paper by Xiaoyi Lin et al. [14] Undertakes a comprehensive analysis of computer-aided diagnosis. The expert knowledge of lesion segmentation masks is limited as it is only used during preprocessing or as supervision to guide feature extraction. To improve the utilization of lesion segmentation masks, this study proposes a RS2-net, which get the predicted segmentation probability map from the initial segmentation inference and then reinput to the network for the final classification inference. the semantic information that can be acquired in advance in a shallow network makes the improved classification performance.

The twelfth paper by Feiyang Yu et al. [15] considers necessary to reveal associations with genetic mutations using Deep learning analysis of routine histopathology. However, previous research has mainly concentrated on image patches or tiles, and there is yet to be any investigation into the prediction of aneuploidy utilizing single cell analysis. For this reason, it proposes a single-cell heterogeneity-aware and transformer-guided deep learning framework to predict aneuploidy from whole slide histopathology images. It obtains cell subtype distributions to measure cancer cell heterogeneity and extract morphological features of different cell subtypes. Lastly, a hybrid network is

built to unify cell heterogeneity, morphology, and deep features for aneuploidy prediction.

All twelve papers tackle different but extremely relevant domain vectors of the computational mathematics modeling in cancer analysis. We present and highlight recent advances in mathematical modelling of cancer based on multimodal medical clinical data. And we believe that this special issue will raises the scientific community's awareness of computational mathematical modelling in cancer analysis. Finally, we would like to thank all the authors who submitted their research results to this special issue. We would also like to thank the many experts in the field who participated in the review process and provided the authors with useful suggestions to improve the content and presentation of the article. We are particularly grateful to Professor Dimitrios I. Fotiadis, Editor-in-Chief, and the editorial team for their support and very helpful suggestions and comments during the delicate stages of completing the special issue.

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