Cell Detection in Computational Pathology

Slide 1: Self-introduction

Hi everyone, I'm Hongbo Wei, an MSc student in AI and Computer Science from the University of Birmingham Dubai. Today, we'll explore cell detection in computational pathology - a promising technology that can improve efficiency for pathologists, leading to better patient care and potentially lower costs. We'll delve into the main highlights of the topic within the context of the state-of-the-art (SOTA), the main applications, the main open questions, technical challenges, and future development.

Slide 2: What are the main highlights of the topic

The field of computational pathology leverages cell detection to analyze digital scans of tissue samples. This technology empowers pathologists in diagnosing diseases like cancer by aiding in the identification of specific cancer subtypes and grades. This increasing demand for accurate diagnoses is colliding with a critical shortage of pathologists [1]. Traditional cell detection methods remain manual and time-consuming, creating a bottleneck in pathology workflows.

Cell detection offers a powerful solution to these challenges. It utilizes high-resolution digital images of entire tissue sections, called whole slide images (WSIs). Due to the large size of WSIs and the memory constraints of contemporary GPUs, techniques like patching are applied to make them suitable for computational tasks. By leveraging Convolutional Neural Networks (CNNs) based on architectures like HoVer-Net, cell detection can automatically identify and locate individual cells within a WSI. It automates the tedious task of manual cell counting, freeing up valuable time for pathologists to focus on complex cases and patient consultations. Automating cell identification leads to greater consistency and accuracy compared to manual methods, which is crucial for a reliable diagnosis. Cell detection holds immense potential to transform pathology workflows by addressing workload limitations, improving efficiency, reducing medical costs, and aiding in better patient care. It also facilitates the quantitative analysis of various cell features like size, shape, and intensity. This data provides valuable insights into disease progression and helps predict patient outcomes. Aiding with tasks like cancer diagnosis, treatment planning, and prognosis prediction. The workflow of cell detection in computational pathology begins with the acquisition of Whole

Slide Images (WSIs) as the source data. These WSIs are high-resolution digital scans that capture entire tissue sections, obtained using advanced slide scanning technologies. Due to the substantial size of WSIs and the memory constraints of contemporary GPUs, various strategies are implemented to render them suitable for computational analysis (One approach involves dividing the WSIs into smaller patches that can be processed individually [2, 3]. Alternatively, neural networks can be used for compressing the WSIs, reducing their memory footprint [4]. Another approach is decomposing the end-to-end training procedure utilizing WSIs into smaller components in conjunction with employing gradient checkpointing to temporarily store intermediate outcomes [5]). Following this, Convolutional Neural Networks (CNNs) are utilized for the automatic detection and annotation of individual cells within the WSIs.

Deep CNNs have emerged as the leading approach for cell detection in computational pathology. These sophisticated networks surpass the previous state-of-the-art methods primarily using machine learning based on handcrafted features [1]. U-Net architecture excels in medical image segmentation tasks, leveraged by the concepts of the Fully Convolutional Network (FCN). However, U-Net still faces challenges in separating neighboring objects and can be sensitive to specific loss function parameters. Here, we propose a new approach that addresses these limitations. HoVer-Net architecture is specifically designed for cell detection in computational pathology, and it achieves high accuracy and effectively addresses clustered nuclei [6]. Cell detection holds immense potential to transform pathology workflows by addressing workload limitations, improving efficiency, reducing medical costs, and aiding in better patient care.

Slide 3: What are the main applications?

Cell detection is revolutionizing pathology, offering a powerful toolset for diverse applications: cancer diagnosis, prognosis prediction, immunotherapy, and drug discovery. At the core of this technology lies the ability to identify regions of interest (ROIs) in cells. These algorithms can then pinpoint areas with abnormal characteristics, like enlarged or misshapen nuclei, which can be indicative of malignant tumors. This information is crucial for both cancer detection and grading [6]. In immunohistochemistry (IHC) analysis, specific proteins are stained within cells. Cell detection facilitates this process by identifying and quantifying these stained cells [7]. This information is vital for tumor subtyping and prognostic biomarker discovery. Beyond cancer diagnosis, cell detection

also plays a critical role in drug discovery and immunotherapy. In drug discovery, cell detection allows us to analyze cellular responses to potential drug candidates, accelerating the development of new therapies. Similarly, quantifying immune cells infiltrating tumors helps assess a patient's eligibility for and predict response to immunotherapy treatments.

These diverse applications showcase the transformative potential of cell detection in pathology. It offers a powerful and versatile toolset for a wide range of diagnostic, prognostic, and therapeutic endeavors.

Slide 4: What are the main open questions?

As we delve deeper into CPath, some critical open questions demand our attention. While AI advancements raise questions about replacing pathologists, the reality is AI is more likely to become a helpful partner. Pathologists' expertise goes beyond analyzing slides. They integrate various data, medical knowledge, and patient specifics for diagnosis and clear communication. AI can currently assist with repetitive tasks, freeing pathologists' time for these crucial areas [1].

Apart from that, generalizability remains a challenge, as models might not perform well on data not included in their training. According to Graham et al. [7], while U-Net architecture performs poorly with unseen data in experimental cases, HoVer-Net architecture can successfully generalize to unseen data.

Furthermore, lack of data is a major hurdle in cell detection for computational pathology. What strategies can be employed to address the limited data problem? Use a specifically designed dataset, for example, the OCELOT dataset, is dedicated to studying cell-tissue relationships for cell detection in histopathology [8]. It is proven that it contributes to cell detection models with improvement in F1-score, and it can aid pathologists in understanding the relationship between cells and their surrounding tissue context for accurate cell detection. Besides, we can apply data augmentation to create larger, more diverse datasets for cell detection tasks [9]. Commonly used methods include mirroring, flipping, random cropping, rotations, warping, addition of noise, and color changes.

Finally, how and when can we close the gap of adopting and integrating these algorithms in clinical practice? Seamlessly integrating cell detection algorithms into existing pathology workflows is essential for practical clinical adoption [9], and this question remains to be further explored. Addressing these open questions will pave the way for the wider adoption of cell detection in clinical settings.

Slide 5: What are the main challenges?

Cell detection in CPath holds immense potential for improving healthcare, but significant challenges must be addressed for wider adoption. Ethical considerations remain paramount. Integrating AI into healthcare necessitates addressing data privacy, security, and potential biases in decision-making (a collaborative effort for data scientists, bioinformaticians, and pathologists). Although regulatory frameworks for AI-powered pathology tools are still evolving, we need to balance patient data security, compliance with regulations (e.g., GDPR), and access to crucial training data [10]. Mitigating potential training data biases and ensuring fair and responsible use are essential, including minimizing bias against specific patient groups and fostering transparency in model decision-making. Apart from this, data scarcity remains a major hurdle for training robust and generalizable cell detection models, one solution is to apply data augmentation to create larger, more diverse datasets for cell detection tasks. Another solution is to foster collaboration across institutions to collect diverse, well-annotated datasets representing various demographics and diseases [11].

Technically, deep learning models, despite impressive results, can be computationally expensive. Developing more efficient algorithms and exploring the efficiency-accuracy trade-off (e.g., model pruning) for cell detection models are crucial for improved computational complexity. Additionally, incorporating mechanisms mimicking pathologists' zooming into diagnostically relevant regions can significantly reduce computation by processing fewer magnifications [11]. Furthermore, 3D pathology tools hold promise in capturing the full tissue structure, potentially mitigating limitations of overlooking important morphological regions in 2D pathology [11].

As for key future developments, there are four main aspects to develop: Firstly (collaboration), fostering closer collaboration between pathologists and computer scientists to ensure CPath tools

are clinically relevant and address actual needs [10]. Secondly (standardization), establishing standardized practices for data processing, storage, and access to facilitate research and development [10]. Thirdly (clinical validation), integrating CPath tools into clinical workflows and validating their effectiveness in real-world settings [10]. Fourthly (clinician buy-in), educating pathologists on using CPath tools effectively while addressing interpretability concerns, and demonstrating cost-effectiveness and improved patient outcomes will encourage adoption [11]. Overcoming these challenges and pursuing these future directions will lead to more efficient workflows, more accurate diagnoses, improved patient care, and ultimately, better health outcomes.

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