A BRIEF STUDY ON HISTOPATHOLOGICAL IMAGES

Rajesh Saturi¹, Prof.P.Prem Chand²

¹Research scholar, Department of computer science & engg, University college of engineering, Osmania university, Hyderabad-500007, Telangana state, India.
²PROFESSOR & Dean, faculty of informatics, Department of Computer Science & Engg, University College of Engineering, Osmania University, Hyderabad-500007 Telangana State, India

Abstract: The process of examining biological tissue under a microscope for detecting the severity of the disease is called histology, it is an essential technique in biomedical research and clinical practice. While slide preparation and imaging is increasingly becoming automated, but the analysis of histology images still require the trained eyes of a pathologist to examine under a microscope. Processing tissues from histopathological images has become now fully computerized, significantly increasing the speed, the labs can produce tissue slides for viewing images digitally. Digitizing these slides, allows pathologist to view these slides on a computer rather than on microscope. Routine analysis of tissues selection will be very difficult, manual task that can be completed only by trained pathologists at a huge cost. In the clinical domain, these methods could improve the accuracy and consistency of diagnoses and hence pathologists can focus on the most difficult cases. This research domain could complete the tasks that are time-consuming for humans, and discover new diseases from millions of whole-slide images (WSIs) or precisely delineating tissues within a tumor, allowing for a quantitative comparison of tumours grown under different conditions.

Keywords: Histopathology, Tumor, Region Of Interest, pathology.

I. INTRODUCTION

The histology process begins, after assessing the history of patient by physical examination, and/or radiographic and laboratory studies, which determine the treatment, that cannot proceed further without histology confirmation. There are several possible approaches for collecting the tissues, including ne-needle aspiration, needle biopsy, excisional biopsy, or excision of the lesion in its entirety. The sensitivity (correct diagnosis) and specificity (incorrect diagnosis) increase from fine-needle aspiration to excision of the entire lesion. This is because the larger biopsies preserve more cellular context and hence the pathologist has to examine multiple slides from different areas of the sample. After biopsy, the pathologist will evaluate the tissue on the macroscopic scale, measuring it and records the information by its characteristics like its colour, shape, size etc.
II. PREVIOUS RESEARCH

In this domain of research, pathologists aim to quantify differences between histology sample slides collected in terms of different parameters like cellular/nuclear morphometry, amount of stroma (the connective tissue cells that support the functions of cells around them) present, types of tissue present, etc. Although some basic analyses can be readily performed using available image analysis software (e.g., Adobe Photoshop, ImageJ [29], or Molecular Devices MetaMorph), most analysis in pathology remains semi-quantitative, staining intensity may be rated as low, moderate, or strong; the amount of a certain cell type may be visually estimated as 0 to 25%, 25 to 50%, or >50% of the total population, and morphometric descriptions of cells are limited to semantic descriptions such as larger, thickened, pleomorphic, or cellular. For some case studies, this type of analysis may not result accurate, because many clinically or biologically relevant features cannot be easily captured and processed by human visual system. For example, given two tumours, how would a pathologist support the claim that the average nucleus size is different between them? Similarly, how can pathologists quantify complex patterns such as chromatin distribution? Automated analysis of histology images would allow researchers to perform these types of quantifications.

| S.NO | AUTHORS | FOCUSED |
|------|---------|---------|
| 1    | Lamia Jaafar Belaid and Walid Mourou, "Image segmentation: a watershed transformation algorithm", Image Anal Stereol 2009;28:93-102. | Analysis of histology images including H&E images as well as fluorescence and multispectral images. It covers pre-processing, segmentation of glands, nuclei, and other sub-cellular components, feature extraction, dimensionality reduction, and classification. |
| 2    | Gowri Srinivasa, Matthew C. Fickus, Yusong Guo, Adam D. Linstedt, Jelena Kovacevic, "Active mask segmentation of fluorescence microscope images," IEEE Transactions On Image Processing, vol. 18(8), pp. 1817-1829, | Issues of data and ground truth collection, including variation among experts and publicly available datasets, and describes automated analysis primarily from a statistical pattern recognition viewpoint. |
### III. EXTRACTING REGION OF INTEREST (ROI)

Recent advancement of digital pathology in medical sciences, mostly influencing the application of digital image analysis. Region of interest extraction (ROI) is an essential step to be performed to distinguish between pathological tissues, to provide information such as tumor from normal tissue and the prognostic information like, invasive ductal carcinoma (IDC) of the breast. Usually a single biopsy can be acceptable for generating dozens of WSIs with high resolution, but entire quantity of the tissues extracted are not useful for diagnosis purpose, only a small portion of tissues extracted from entire quantity is used. Hence a faster mechanism is required to extract these ROIs from histopathology images. Once these interested areas are detected and identified, then the extracted portions of the tissues can be provided to the pathologist’s in order to carry out the further procedure for diagnosis. A system with high potential of extracting good region of interest will certainly maximize the efficiency. Hence based on this concept, a review on ROI extraction is collected from different sources.

Most of the technical researches and medical investigators had already done research and successful in the domain of ROI extraction which is very efficient and effective to computerize the complete system.

| 3 | Chao-Hui Huang, Antoine Veillard, Ludovic Roux, Nicolas Lomenie, and Daniel Racoceanu, “Time-efficient sparse analysis of histopathological whole slide images,” Computerized Medical Imaging and Graphics, Elsevier, vol. 35, pp. 579–591, December 2011. | WSI informatics including quality control during image acquisition, feature extraction, region of interest (ROI) detection, and visualization |
| 4 | P. Ghosh, S.K. Antani, L.R. Long, G.R. Thoma, "Unsupervised Grow-Cut: Cellular Automata-Based Medical Image Segmentation," First IEEE International Conference on Healthcare Informatics, Imaging and Systems Biology, pp. 40-47, July 2011. | Breast cancer histology image analysis, including both H&E and immune histochemical (IHC) stains |

![Fig 2: ROI extraction](image-url)
One of the approach is to select a sample input with low resolution which can be used to extract various features based on its color and sparse coding of the sub-patches. These are then classified using Support Vector Machines (SVM) to detect ROIs. [23]

- Similarly another approach is to process the image at different multiple scales and then a color clustering is used to recursively partitioned the images of the breast cancer tissue at increasingly fine resolutions accurately and efficiently to identify lesions Vs normal regions and tissue Vs non-tissue [24].

- Bilge et. al [1] proposed a method which is carried out by tissue microarray deficiency for identifying automatically the region of interest(ROI) with adaptive image segmentation which involves color and gray scale image segmentation. Here texture parameters of segmented histology image blocks are represented with three parameters of the image, covered by chromatin-rich cell nuclei (B), percentage occupied by collagen-rich stroma (P), a parameter of spatial heterogeneity (H), and a statistical learning algorithm is developed to classify the image blocks into Normal-specific, Cancer-specific and Non-specific.

- Egzi et. al [2] mainly focused on the localization of diagnostically relevant regions of interest (ROI) in whole slide images(WSI). The primary goal is to develop an ROI that gives a decision (relevant or non-relevant) for given image windows. It uses the viewport tracking data of three pathologists to generate the training and test samples. And then provided a set of logs for multiple different whole slide images, for which feature vectors to be created and used to classify ROIs. In this paper the method applied will generate a set of rules to identify important actions like zoom-in, zoom-out, panning and fixation in the viewport logs. Using these viewports, a binary model is trained using logistic regression and support vector machines for predicting ROIs in new images.

- Yassine et. al [3] aims to show a fully automated approach for ROI based on multi-agent system which incorporates spatio temporal interest point of detection on images by using HOG 3D descriptor for agent initialization.

- Y. Aribi et. al [4] described an algorithm known as REGION_GROW which was used for partial automatic tracing of ROI .

- In another attempt Y.Aribi et al [6] developed a semi-automatic system based on fast marching method for ROI segmentation. In this automatic approach, the user has absolutely no intervention.

- Daniel Stahl et. al [7] used the concept of compartments and developed a fully automated system for segmentation of kidneys and detecting the non-functional regions of the kidney.

- Sushmita et. al. [9] discusses segmentation and general image processing operations like filtering, interpolation, histogram estimation along with the soft computing strategies for ROI extraction. Here the author discusses 3 main categories for ROI extraction First generation, Second generation and Third generation algorithm.

- MichealDerde et. al. [10] introduced a general purpose framework which is capable of solving problems that are not restricted to a specific task and can analyze the local information related to microscopic images succeeded by interaction with physicians in addition to considering direct feedback. The feedback is general capable of adapting learning models and tasks, to detect the region of interest.

- N.R. Pal et.al. [11] and M.N. Gurcan et.al. [12] Presented a comprehensive study on various segmentation techniques for extracting ROI. Various types of segmentation techniques are discussed on on extracting ROI, techniques like intensity or color-thresholding, further classified as multi-thresholding or bi-level thresholding. Recent ROI extraction techniques are more focused on automated approaches that mainly depend on machine learning techniques. Such type of automated approach for ROI extraction is described in [19] where huge amount of data is processed and interesting patterns are extracted.
RaduRogojanu et. al. [15] used region growing based methods for ROI extraction automatically.
R. Szeliski et. al. [18] proposed some energy based method for the same.
Finally, the work in [22] used random forests technique to classify pixels belongs to a fixed set of predefined classes and employs regression trees to learn meaningful thresholds which are then used for segmenting the image.

Since histopathological image analysis is essentially a cross-disciplinary area, where there are unique challenges in distribution of research results. But there are a few journals that are focus on automated analysis of medical images, the majority of histopathological image analysis published in the journals of researcher’s fieldlike (pathology, computer vision, etc.). Hence there is a need for more support regarding the clinical research and significance of automated histopathology image analysis methods. Its very difficult to compare various methods presented in the literature, since individual researcher used their own dataset and presented their results using different metrics. Therefore there is a huge need for standard datasets and ground truth for verification and validation of these methods. For example, a researcher at University of South Florida had put together a database of digital mammograms [1]. Although the variety of conditions studied in histopathology image analysis is greater, but it is still important that standard datasets standard metrics are to be compiled for greater performance. This allows for direct comparison of the variety of analysis methods being reported in the literature. An additional difficulty is the variety of analyses performed on the histopathological images.

IV. CONCLUSION

Histopathology plays a crucial role in medical imaging, hence an automated histopathology image analysis shows deep impact on the cost, quality and availability of the entire healthcare domain. ROI extraction is one of the primary step for entire automation, about which a detailed review has been carried out in this paper. ROI is the actual investigation area in the entire slide image. Wide range work has already been carried out in this domain, which is already mentioned in the related works. The above discussed methodologies like thresholding, active contour etc., were later improvised and refined upon using advanced methods of fuzzy logic, soft computing etc. but the clinical acceptance of these type of methods is still a disputed matter. The generalization of this technique for automation is still required to be accomplished. Most of the existing technique is proficient in handling a single area of concentration. Extraction of ROI or discriminative area will serve as a consent for the entire histopathological image analysis. Currently mobile devices, tablets and smart phones plays an important role in every individual’s life. Mounting this kind of application on these devices would probably enhance the point of view of diagnosis and treatment by the pathologist or any expert at any place and at any time easily just by a single click. This will be an great support for the medical practitioners in delivering and rendering accurate, faster diagnosis to the suffering individuals.

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