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（博士課程）
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論 文 要 旨
THESIS SUMMARY

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要旨（英文 800 語程度）
Thesis Summary（approx.800 English Words ）

In recent years, along with the development of computational power and image processing, a new field called digital pathology has been developed to aid pathologist in diagnosing disease. In this field, the tissue (histological) or cell (cytological) samples taken are from patients are digitally imaged through slide scanning system instead of observed through microscope. Then, features such as morphological structure, tissue pattern are extracted from the images using image processing algorithm. Using these data, an automated classification system can be developed to identify the severity of the disease. This technique is beneficial to create a fast and accurate diagnosis pipeline, helping the pathologist and ensuring better life expectancy for patients.

Nevertheless, there are still many challenges and problems that need to be tackled in digital pathology. For example, current imaging system and algorithm developed for digital pathology centralize around color image. Thus, the samples still need to go through standard staining procedure which can be time consuming. Fortunately, there are several studies that have been done to integrate quantitative phase imaging such as digital holography into digital pathology. This method does not require staining procedure as the imaging principle is based material's refractive index instead of absorption. Despite this efforts, current works only focus on integrated phase while textural features that are widely used in color image are not yet fully explored in phase image. Moreover, because most studies in phase imaging centered on live transparent cells and not stained tissue or cells, the relationship between phase and color information in histological sample is not well known. Another challenge is when imaging thick samples, scanner that has low depth of field will require multiple acquisition in Z-axis. Digital holography could offer image refocusing from a single digital hologram, but it only works for coherent image.

In this study, a hybrid optical system that combines incoherent (bright-field) and coherent (digital holography) imaging was developed. This system is used to capture the color image and digital hologram of stained cytological sample (malignant lymphocytes) and the phase distribution was analyzed. The color image is used to assist segmentation process of the overlapping cells. From the experimental analysis, the spatially-averaged phase mean value of malignant lymphocytes has larger dispersion compared to normal cells. This information can be exploited for malignant lymphoma identification in digital pathology. The study also confirmed that the cell phase value is correlated with its size, regardless the cells are stained and enclosed in mounting media.

Next, an analysis of quantitative phase of Hematoxylin and Eosin stained histological sample was conducted. Here, using previously mentioned hybrid imaging system, the phase and color image of liver tissue were captured. After that, the relationship between phase and color textural information inside nuclear region was investigated. From the analysis, this study discovered that texture features obtained from phase image could provide different

information from the color image. The most apparent distinction between normal and cancer nuclei in phase image was observed in the Grey-Level Co-occurrence Matrix contrast and homogeneity. This unique feature is beneficial for classifying the liver tissue into Hepatocellular Carcinoma (HCC) or normal cases. Another advantage in using phase image in classification is the possibility of using unstained samples, thus faster pathological diagnosis can be conducted.

Finally, by taking the advantage of the hybrid coherent and incoherent imaging system, a novel image processing technique was developed. This method enables 3-D reconstruction and refocusing of color object from bright-field image by using information from digital holography as support. The algorithm exploits the sparsity of the 3D objects and reconstruct it from digital hologram using compressive holography. Next, a binary mask is created to separate the object from transparent voxels. The binary mask is then used to assist 3-D color object reconstruction from a bright-field image. After that, image refocusing can be conducted by applying convolution operator between the reconstructed object and the 3-D point spread function. The effectiveness of this algorithm was demonstrated in a simulation of simple object and cytological cells phantoms. In these simulations, the reconstructed objects achieved good match with ground truth. This method has potential to be applied for 3-D pathological imaging without requiring the acquisition of z-stack images.

As for conclusion, this study explored the application of quantitative phase image via digital holography for both cytological and histological samples by developing a hybrid coherent and incoherent imaging system. For cyto-pathological field, this study contributed in the identification of malignant lymphocytes from phase distribution of stained sample. For histo-pathological field, this study explored the unique textural feature in phase image and its application in classifying HCC cases and the possibility of using unstained sample in diagnosis. Lastly, this study developed a novel 3-D reconstruction algorithm for application in imaging thick samples in digital pathology.

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