Improving the sub-image classification of invasive ductal carcinoma in histology images

Khanabhorn Kawattikul[1], Kodchanipa Sermsai[1], Phatthanaphong Chomphuwiset[2]
[1]Department of Information Technology, Faculty of Social Technology, Rajamangala University of Technology Tawan-ok, Chanthaburi Campus, Chanthaburi, Thailand
[2]Department of Computer Science, Faculty of Informatics, Mahasarakham University, Maha Sarakham, Thailand

Article Info

Article history:

Received Apr 14, 2021
Revised Jan 28, 2022
Accepted Feb 7, 2022

Keywords:

Breast cancer classification
Computer aided diagnosis
Deep neural network
Histopathology image analysis
Morphological features

ABSTRACT

Whole slide image (WSI) processing is a common technique used in the analysis process performed by pathologists. Identifying precise and accurate regions of cancerous in the tissue is an important process in the disease diagnosis modality. This work proposes an automated technique for identifying invasive ductal carcinoma (IDC) in histology images using. An image is divided into small non-overlapped patches (or image windows). Then, the task is to classify the image patches into different classes, i.e., i) IDC and ii) non-IDC. We employ a two-stage classification-based to classify the patches, as to identify IDC regions in the tissue. In the first stage (patch-level classification), image patch classification is carried out using a conventional handcrafted feature and deep-learning technique are explored. The second stage (post-processing) undergoes a refinement process, which considers the spatial relationships between the neighboring patches. This stage aims to amend some of miss-classified patches. Markov random field (MRF) is implemented in this stage to examine the relationships of the patches and their neighborhoods. The experiments are conducted on public dataset. The experimental results show the post-processing can improve the performance of the classification in the first stage using the handcrafted-based technique and deep learning.

Corresponding Author:

Phatthanaphong Chomphuwiset
Department of Computer Science, Faculty of Informatics, Mahasarakham University
Maha Sarakham, Thailand
Email: phatthanaphong.c@msu.ac.th

1. INTRODUCTION

Histology image analysis is a clinical procedure that is performed to study and understand the histology of tissue samples. In the conventional process, tissue samples are collected from body organs. Then, a sequence of the preparation process is carried out (i.e., fixation, dehydration, clearing, infiltration, embedding, sectioning, and staining) [1]-[4]. After the preparation process, they are mounted to glass slides for the examination under a light microscope. A whole slide analysis is a common technique that has been applied during examination process (by pathologists). The examination is usually performed with various magnifications (different scales) to obtain an essential meaningful interpretation of tissue histology. The invention of digital tissue images has immensely contributed to the modern pathology that allows pathologists to be able to perform their tasks in examining and analyzing the digital tissue slides in many diagnostic applications [5]. As a result, the analysis for disease prognosis and progression can be carried out more expediently and productively. This includes, for example, disease prognosis, severity and malignancy level evaluation, and tissue stating and grading. Associating with clinical data of patients, further proper treatment can be, as a consequence, planned efficiently.

In modern histology image analysis, an automated process of screening systems assists pathologists in the diagnosis modality. Invasive ductal carcinoma (IDC) is the most common subtype of all breast cancer (BCa) is an example [6]. Identifying IDC in the tissue images can be substantial to help in the diagnosis process and evaluate the severity of cancer. In the WSI examination, the resolution of the image imposes the handwork that is required in the analysis process. With the emergence of AI and technology, an automated system for identifying IDC in the tissue images can be implemented [7]-[11]. In general, the identification can be carried out using a classification-based technique. The image of tissues is divided into non-overlapped patches. Each of the patches is then fed to a classifier to identify whether it is IDC or vice versa. Therefore, this work proposes a two-stage classification-based to classify the patches, and yet to identify IDC regions the tissue. In the first stage, image patch classification is carried out using a conventional handcrafted feature (based around on texture descriptors) and deep-learning techniques are explored. The second stage undergoes a refinement process, which considers the spatial relationships between the neighboring patches. This stage aims to adjust the miss-classified patches to correct classes. Markov random field (MRF) is implemented in this stage, taking into account the relationships of the neighboring patches [12], [13].

The rest of this paper is organized as follows: section 2 provides related work and the literature in histological image analysis techniques. Section 3 explains the proposed technique of classifying the patches using i) conventional feature extraction and learning algorithms, ii) knowledge transferring approaches using deep learning-based methods, and iii) in-cooperating spatial information of the patches in the classification. Section 4 provides the experimental results and the evaluation of the proposed method before the conclusion is given in section 5.

2. RELATED WORKS

Artificial intelligence (AI) pathology for digital pathological image analysis is usually developed by applying image processing and machine learning techniques to implement computer aided diagnosis (CAD) applications aiming at assisting pathologists to perform their tasks [1]. These applications are usually decomposed by different level-of processing, ranging from low-level processing (e.g., detecting and segmentation [14], [15]) and high-level analysis (e.g., disease stating, classification and quantitative assessment of tissues [6]-[11], [16]-[22]).

Detecting and segmenting cellular structures in the images is one of low-level processes that is usually required for further high-level analysis, e.g., extracting structure semantics for the analysis. Color and morphology-based approaches have been reported in the literature as the pioneer techniques applied to detect or segment the structures in histology images [5], [23]. These techniques are not able to produce promising results as they cannot cope with the variation of histology images resulted from the preparing process, for instance, uneven staining. Watershed and Level-Set technique have also been one of the alternative methods applied in the low-level state for detecting some important cellular structures in the images [5]. This computational method usually confronts a number of problems, e.g., seed initialization and touching cellular structures; therefore, the technique is not able to produce promising results and computational burden [23]. As deep learning is increasingly becoming method that have been implemented in various computer vision application, including histological image analysis [15]-[16], [23]-[25]. The technique, e.g., U-Net, has applied to detect different types of cellular, e.g., cell nuclei, blood vessels, epithelium, and lymphocytes [24]. The deep learning approaches have reported for producing promising outcomes in detecting some cellular structures in the images.

Tissue classification is one of the common tasks in histology image analysis that has been in the attention of the community. The classification can generally be used in the detection process [10], [11], [17]-[22]. Textural features are one of the techniques that have been applied in the classification process [1]. These handcrafted feature extractors are performed to represent local/global appearance of the image before they are fed to leaning algorithms [1]. In recent years, ensemble-based techniques have also been introduced to improve the performance of a single classifier. With the variation of the images (color, light, scale, and conventional variation), the handcrafted-based technique can produce promising results in some dataset [1]. Deep learning (DL) have been applied to the tasks in histology image analysis, including classification process [10], [17]-[20].

VGG16 (CNN architecture) have been used in classifying sub-image of histopathological, image into different types, such as IDC and non-IDC [9]. The work divides the whole image into small non-overlapped sub-images. Each of the patches is fed to the trained model (by VGG16). They report some promising results in the classification on a public dataset. N. Brancati *et.al.* propose a technique for Breast Invasive Ductal Carcinoma Detection and Lymphoma using a deep learning technique [10]. They employ

FusionNet (a residual convolutional neural network) to performance the classification in the image patches that have been partitioned from the whole slides. The classification is carried out to classify the image patches into IDC and non-IDC, associate with three classes of lymphoma sub-types.

The classification on sub-images of the whole-slide histology images can be improved by determining the relationships of a sub-image (image patch) with its neighboring patches. The type of the patch (in a certain scale) tends to be marginally the same with the patches around it. Therefore, this paper is aimed at constructing a post-processing method that examines the relationships of the patches for improving the classification performance.

3. DATA AND METHOD

Invasive ductal carcinoma (IDC) is a common subtypes of all breast cancers [6]. In practice, the evaluation the aggressiveness grade of the sample is performed by the specialist pathologists that examine mounted samples on the regions typically contain with the IDC. Therefore, one of the common tasks for automatedly determine the aggressiveness grades of the tissue is to delineate the exact regions of IDC inside of a whole mount slide. This section describes the technique for classifying the image patches.

3.1. Data description

Classifying image patches in histology images of breast histology. A histology image of breast tissue is separated into small image patches (image widows) with equal size. Each of image patch (p) will be classified into two types, i.e., invasive ductal carcinoma (IDC) or negative patch and non-invasive ductal carcinoma (non-IDC) or positive patch. An example is depicted in Figures 1(a) and 1(b).

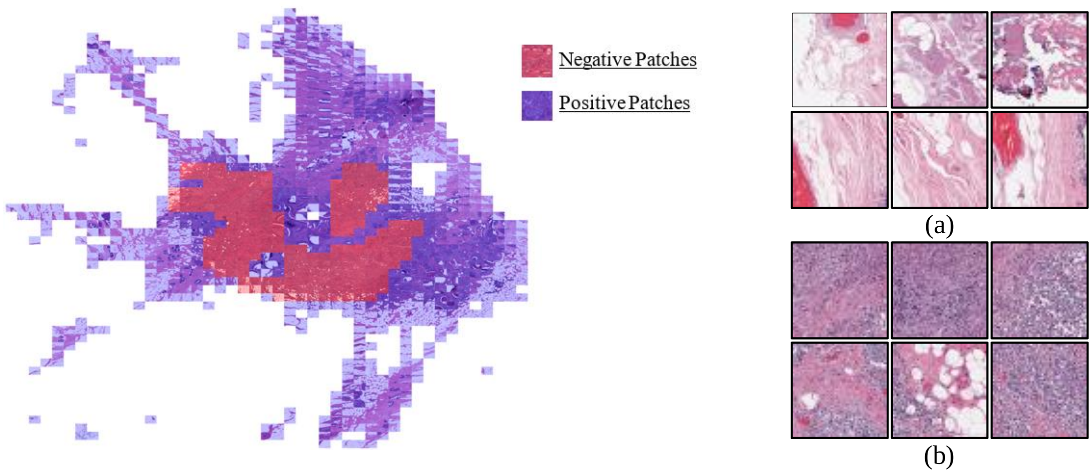


Figure 1. Example of patches in a whole slide image of breast histology. The patches are classified into 2 classes (by the experts), i.e., (a) IDC and (b) Non-IDC [3]

Thid work uses a public dataset [9], [10] comprising 72,120 image of positive and negative IDC. The image patches are collected from several slides undergoing breast cancer at x5 of resolution. Background patches are eradicated from the dataset (see Figure 1).

3.2. Patch-level classification

Classifying the image patches is straightforward. In general scheme of classification methods, a set of objective features ($\phi(x) \in R^d$) is firstly extracted from a patch. The classification can be formed by constructing a learning function ($f: \phi(t) \mapsto C$) that maps the input features ($\phi(t)$) to a patch class (C). The mapping function can be implemented in many forms. In this work, two techniques of classification are applied, i.e., conventional machine-learning method and deep learning-based method [Joseph]. Conventional machine-learning method.

Handcrafted feature for classification textural features, i.e., Grayscale level cooccurrence matrix (GLCM) and HOG [26], [27] are implemented in this work. An image patch is converted to a grayscale image before the texture-features are extracted, $\phi(x)$. The classification on the extracted features is performed using a Random Forest classifier that classifies that patch into 2 types, $f: \phi(t) \mapsto C$.

Deep leaning classification in general, CNNs have demonstrated a success and drawn to the classification problem. The techniques model a learning function that computationally maps an input image $t \in R^{h \times w \times d}$ (where h and w is the image resolution and d is the image depth) in output probability vectors $y \in R^{C}$, C is the number of classes, in this work $C = 2$ (i.e., IDC and non-IDC). Each layer, (l), of the architecture derives a transformation module, which is associated with a set of adjustable parameters followed by non-linear operation, call activation process:

$$t_l = f_l(W_l * t_{l-1} + b_l), \tag{1}$$

where $1 \leq l \leq L$ denotes the layer index and L is the number of layers in the networks, t_0 is an input image, W_l and b_l are model parameters at layer l, and $*$ denotes a convolution operator with pre-defined kernels for convolution layers. f_l is a layer specific non-linearity (i.e. defined by activation functions), composed of Rectify Linear Unit (ReLU), which is defined as (2):

$$ReLU(t_l) = (\ max(0, t_l), \tag{2}$$

and max-pooling mechanism-a local response normalization-or drop-out. The output of the last layer, p_L, is input to a softmax function, which outputs a probability vector over the target classes. The classification can be performed by minimizing a loss function with respect the network weights (w) as (3).

$$\underset{w}{\operatorname{argmin}}\, L(\phi(p), W) \tag{3}$$

The loss function (L) is evaluated by determining the difference of the prediction obtained by the network (W) and the ground truth data or targets. This loss function can be implemented using different techniques, for instance, square loss, logistic loss, exponential loss, and hinge loss. To generalize the network, an optimization technique is applied through training processes. Examples of the optimization techniques are Stochastic Gradient Descent, RMSProp and Adam [18]. DiagramVGG16 (CNN architecture) as shown in Figure 2.

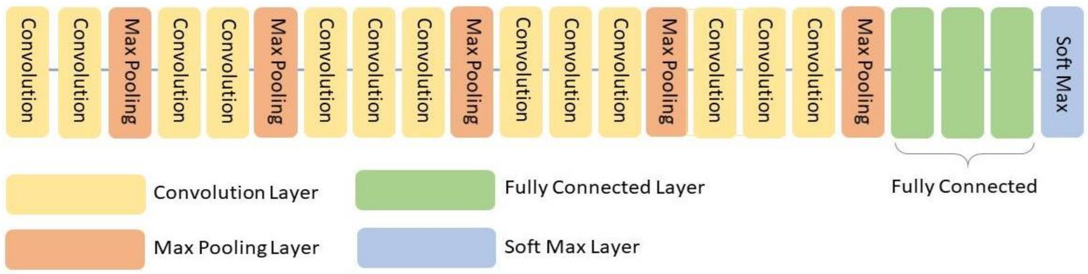


Figure 2. Diagram of VGG16 architecture [28]

3.3. Integrating spatial location of patches

After the classifiation is peformed, this work impleement Markov random field to refine the classification results. The technique examines the relationships of the patch images and its neighbors [12]. For a given set of the patch image in an image, there exists an associated probability $P(C|p)$--where C is the class of patch types (IDC and Non_IDC), which is obtained from the classification carried out in the previous process. This probability is exploited as a prior probability in MRF process. Then, an inference is caried out using graph cut techniques to obtain the final classification, as the refinement procedure. Given a set of image patches W, we can define a lattice graph and generated it as shown in Figures 3(a) and (b). The edge $e_{i,j}$ defines the adjacency of pair of the patches i and j in the graph. To obtain a final classification, an energy function is defined as:

$$E(G) = E_s + E_d(.) \tag{4}$$

where E_s denotes a function that examines the smoothness of the connected nodes. This energy term usually preserves the discontinuity at the boundary between classes. E_s is defined as (5):

$$\mathrm{E}_s = \sum_{\{i,j \in \mathrm{N}, i \neq j\}} \mathrm{V}(p_i, p_j), \tag{5}$$

where V is a smoothing function preserving the relation of the connected patches. $\mathrm{V}(\mathrm{p}_i, \mathrm{p}_i)$ is calculated based on radial-based function, which is defined as (6):

$$\mathrm{V}(p_i, p_i) = \mathrm{e}^{\left\{-\frac{\|p_i - p_j\|^2}{2\sigma^2}\right\}} \tag{6}$$

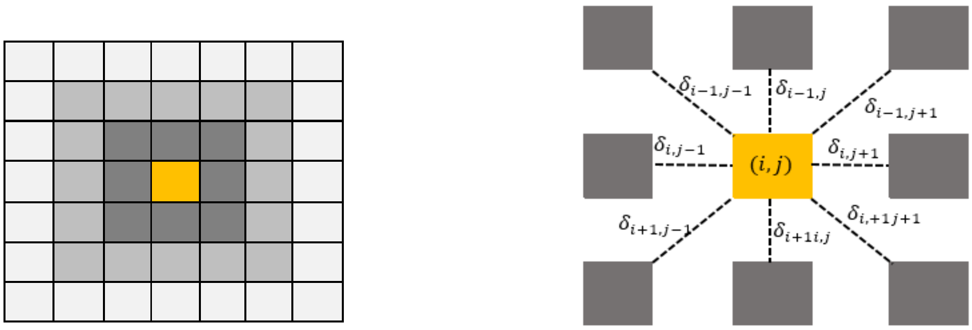
where σ signifies the offset of the relation between the image patches. In this work, the data term is designated by using the posterior probability of the classification performed in the previous step.

$$E_d = \sum_{p \in S} D(p) \tag{7}$$

The energy function shown in (4) will be minimized subjecting to the class label (C) to obtain the optimal results, as the final classification decisions. Therefore, the data term is calculated based on a function defined as (8).

$$D(s) = -\log(c|s) \tag{8}$$

To obtain the final classification decision, the optimization is carried out using the graphcut technique [22].



(a) (b)

Figure 3. Example of the relation of image patches in the image slides; (a) the spatial relationships of a patch and its neighbors bases on a distance metric and (b) the 8-neigbor of the patch

4. EXPERIMENTAL EVALUATIONS

4.1. Experimental setup

The image patches (from the whole slide) are prepared. Background patches are removed from the dataset using a simple thresholding method on the normalized image patches [0-1]. The threshold (τ) is set to 0.2 where the original background is 0. All the image patches are divided into 2 set, i.e., IDC and non-IDC. The dataset is imbalanced when negative patches are greater than positive patches. The data is separated into 2 sets, 70% of the dataset is the training and validation set, and 30% is folded as the test data.

4.2. Experimental result and discussion

The experiments are conducted to evaluate that performance of the proposed method. The handcrafted features are generated on the dataset (explained in section 3.) before the classification is carried out by a random forest. The experiment varies the size of a number of trees in the random forest to observe the sensitivity of the classifier. The classification results are demonstrated in Table 1.

Table 1. The results of the classification obtained from the handcrafted-features (textural features and HOG) and a random forest with a various number of trees

	No. of Trees = 50		No. of Trees = 75		No. of Trees = 100		No. of Trees = 125	
	precision	recall	precision	recall	precision	recall	precision	recall
GLCM	0.75	0.72	0.78	0.71	0.76	0.73	0.77	0.75
HOG	0.69	0.70	0.75	0.75	0.71	0.74	0.74	0.72

From Table 1, the precision and recall value (average over two classes) obtained from different size of the Random Forest are marginally the same. GLCM produces better results, in overall, than HOG. No. Using GLCM, No. of Trees (NoT)=75 outcomes the best precision (0.78) yet produce low recall (0.71) comparing to NoT=125 (which is 0.75). Therefore NoT=125 will be used for the comparison the later experiments. The CNN (explained in section 3) is implemented. The defaults parameter of VGG16 is employed to construct the network. The training and testing are performed on the prepared dataset and the resulted is shown in Table 2.

Table 2 show the results collected from using VGG16 (in the classification process). The results demonstrate the deep learning implemented in this work outperforms to the handcrafted features shown in Table 1. The precision and recall values are increased up 4-6%. To evaluate the performance of the proposed method, the last experiment is run on the same dataset. The post-processing (explained in section 3) is implemented. The classification in the single patch-level classification is deployed in the optimization process using the graph-cut technique. The results are shown in Table 3. The results in Table 3. show that pre-processing technique that use the relationships between the patches can improve the performance of the classification.

Table 2. The results of the classification obtained VGG16

	Positive		Negative		Average	
	Precision	Recall	Precision	Recall	Precision	Recall
Validate Set	0.89	0.87	0.82	0.82	0.85	0.84
Test Set	0.84	0.82	0.79	0.81	0.81	0.81

Table 3. The results of the classification obtained from the post-processing process by integrating the spatial relationships of the image patches

	Single Classification		Post-Processing	
	Precision	Recall	Precision	Recall
VGG16	0.81	0.81	**0.85**	**0.82**
GLCM+RF	0.77	0.75	**0.81**	**0.82**
HOG+RF	0.75	0.75	**0.79**	**0.78**

5. DISCUSSION

Identifying the region of cancerous arears can be achieved by implementing a classification technique. This work tries to solve a binary-class classification by dividing the whole slide into two areas, IDC, and Non-IDC. Therefore, the image is separated into small non-overlapped patches. From visual inspection, there some subtle different of appearance of the patches. Therefore, a textural feature is used. GLCM can deliberately present the overall appearance of the patches and result fair outcomes. The precision and recall of the two is around 75-77%. Considering the results, GLCM and HOG produce low recall in negative samples (70%). This may not be applicable in implementing the technique in actual screening system, where we try to highlight the cancerous region for the pathologists. In addition to the handcrafted features, Table 2 demonstrates the results obtained from the deep learning method (using VGG16). From the observation, VGG16 produces marginally good results. It obtains 82% of recall on negative samples and results good outcome for positive samples. The technique generates the abstraction of the features (deep features) from the images, which increases the discrimination degree in this binary-class problem.

Table 3 demonstrates the importance of applying the spatial relationships of the patches (location and the output from the classification) in the whole slide images. Miss-classification can be found throughout the patch-level classification. The post-processing is implemented to correct the miss-classified patches from the classification. The results indicate that around 4% of miss-classified patches are corrected. These image patches are assigned a class label based on the result of the patch-level classification. The classification result of the two class can be very subtle for this binary-class problem, for example 0.49 for IDC and 0.51 for Non-IDC. Therefore, apply the spatial location of the patches tends to improve the performance, as a sing patch label is likely to be identical to the patches around it.

6. CONCLUSION

Invasive ductal carcinoma (IDC) is the most common subtype of all breast cancers. In general, pathologists identify IDC in the tissue images and evaluate the severity of the tissues. In addition, identifying IDC in the slides is a challenging task, as the appearance of IDC can be subtle to other regions/areas. This work proposes an automated technique for identifying IDC in the tissue images using a classification technique. A tissue image divided into small non-overlapped patches (or image windows). Then, the task is to classify the image patches into different classes, i.e., (i) IDC and (ii) non-IDC. This work employs a two-stage classification-based to classify the patches, as to identify IDC regions in the tissue. In the first stage (patch-level), image patch classification is carried out using a conventional handcrafted feature (based around on texture descriptors) and deep-learning technique are explored. The second stage undergoes a refinement process, which considers the spatial relationships between the neighboring patches. This stage aims to amend some of miss-classified patches to correct classes. Markov random field (MRF) is implemented in this stage, to take in to account the relationships of the patches nearby. The experiments are conducted on the collected data of the image patches. The experimental results show the post-processing process is superior to the patch-level classification using the handcrafted-based technique and deep learning.

ACKNOWLEDGEMENTS

This research project was financially supported by Mahasarakham University, Thailand.

REFERENCES

[1] M. N. Gurcan *et al*., "Histopathological image analysis: a review," *IEEE Reviews in Biomedical Engineering*, vol. 2, pp. 147-171, 2009, doi: 10.1109/RBME.2009.2034865.

[2] L. Barisoni, K. J. Lafata, S. M. Hewitt, A. Madabhushi, and U. G. J. Balis, "Digital pathology and computational image analysis in nephropathology," *Nature Reviews Nephrology*, vol. 16, pp. 669-685, 2020, doi: 10.1038/s41581-020-0321-6.

[3] J. A. A. Jothi and V. M. A. Rajam, "A survey on automated cancer diagnosis from histopathology images," *Artificial Intelligence Review*, vol. 48**,** pp. 31-81, 2017, doi: 10.1007/s10462-016-9494-6.

[4] A. Das, M. S. Nair, and S. D. Peter, "Computer-aided histopathological image analysis techniques for automated nuclear atypia scoring of breast cancer: a review," *Journal of Digital Imaging*, vol. 33, no. 5, pp. 1091-1121, 2020, doi: 10.1007/s10278-019-00295-z.

[5] S. Wienert *et al*., "Detection and segmentation of cell nuclei in virtual microscopy images: a minimum-model approach," *Scientific Reports*, vol. 2, no. 503, 2012, doi: 10.1038/srep00503.

[6] H.-P. Sinn and H. Kreipe, "A brief overview of the WHO classification of breast tumors, 4th edition, focusing on issues and updates from the 3rd edition," *Breast care (Basel, Switzerland)*, vol. 8, no. 2, pp. 149-154, 2013, doi: 10.1159/000350774.

[7] S. Roy, R. Kumar, V. Mittal, and D. Gupta, "Classification models for invasive ductal carcinoma progression, based on gene expression data-trained supervised machine learning," *Scientific Reports*., vol. 10, no. 4113, 2020, doi: 10.1038/s41598-020-60740-w.

[8] S. Tsutsui, S. Ohno, S. Murakami, A. Kataoka, J. Kinoshita, and Y. Hachitanda., "Histological classification of invasive ductal carcinoma and the biological parameters in breast cancer," *Breast cancer*, vol. 10, no. 2, pp. 149-152, 2003, doi: 10.1007/BF02967640.

[9] F. Siddiqui, S. Gupta, S. Dubey, S. Murtuza, and A. Jain, "Classification and diagnosis of invasive ductal carcinoma using deep learning," in *2020 10th International Conference on Cloud Computing, Data Science & Engineering (Confluence)*, 2020, pp. 242-247, doi: 10.1109/Confluence47617.2020.9058077.

[10] N. Brancati, G. De Pietro, M. Frucci, and D. Riccio, "A deep learning approach for breast invasive ductal carcinoma detection and lymphoma multi-classification in histological images," *IEEE Access*, vol. 7, pp. 44709-44720, 2019, doi: 10.1109/ACCESS.2019.2908724.

[11] C. Zhu, F. Song, Y. Wang, H. Dong, Y. Guo, and J. Liu, "Breast cancer histopathology image classification through assembling multiple compact CNNs," *BMC Medical Informatics and Decision Making*, vol. 19, no. 198, 2019, doi: 10.1186/s12911-019-0913-x.

[12] Z. Wei and H. Li, "A Markov random field model for network-based analysis of genomic data," *Bioinformatics*, vol. 23, no. 12, pp. 1537-1544, 2007, doi: 10.1093/bioinformatics/btm129.

[13] Y. Boykov, O. Veksler, and R. Zabih, "Fast approximate energy minimization via graph cuts," *IEEE Transactions on Pattern Analysis and Machine Intelligence*, vol. 23, no. 11, pp. 1222-1239, Nov. 2001, doi: 10.1109/34.969114.

[14] Ł. Rączkowski, M. Możejko, J. Zambonelli, and E. Szczurek, "ARA: accurate, reliable and active histopathological image classification framework with Bayesian deep learning," *Scientific Reports*, vol. 9, no. 14347, 2019. doi: 10.1038/s41598-019-50587-1.

[15] T. Binder, E. M. Tantaoui, P. Pati, R. Catena, A. S.-Aghayan, and M. Gabrani, "Multi-organ gland segmentation using deep learning," *Frontiers in Medicine*, vol. 6, no. 173, Aug. 2019, doi: 10.3389/fmed.2019.00173.

[16] W. Han *et al.*, "Histologic tissue components provide major cues for machine learning-based prostate cancer detection and grading on prostatectomy specimens," *Scientific Reports*, vol. 10, no. 9911, 2020, doi: 10.1038/s41598-020-66849-2.

[17] O. Iizuka, F. Kanavati, K. Kato, M. Rambeau, K. Arihiro, and M. Tsuneki, "Deep learning models for histopathological classification of gastric and colonic epithelial tumours," *Scientific Reports*, vol. 10, no. 1504, 2020, doi: 10.1038/s41598-020-58467-9.

[18] A. Janowczyk and A. Madabhushi, "Deep learning for digital pathology image analysis: A comprehensive tutorial with selected use cases," *Journal of Pathology Informatics*, vol. 7, no. 29, Jul. 2016, doi: 10.4103/2153-3539.186902.

[19] H. Elmannai, M. Hamdi, and A. AlGarni, "Deep learning models combining for breast cancer histopathology image classification," *International Journal of Computational Intelligence Systems*, vol. 14, no. 1, pp. 1003-1013, 2021, doi: 10.2991/ijcis.d.210301.002.
[20] Y. H. Chang *et al*., "Deep learning based Nucleus Classification in pancreas histological images," in *2017 39th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, 2017, pp. 672-675, doi: 10.1109/EMBC.2017.8036914.
[21] D. Komura and S. Ishikawa, "Machine learning methods for histopathological image analysis," *Computational and Structural Biotechnology Journal*, vol. 16, pp. 34-42, 2018, doi: 10.1016/j.csbj.2018.01.001.
[22] C. Zheng, X. Pan, X. Chen, X. Yang, X. Xin, and L. Su, "An object-based markov random field model with anisotropic penalty for semantic segmentation of high spatial resolution remote sensing imagery," *Remote Sensing*, vol. 11, no. 23, 2019, doi: 10.3390/rs11232878.
[23] Y. Zhang, L. Yang, J. D. MacKenzie, R. Ramachandran, and D. Z. Chen, "A seeding-searching-ensemble method for gland segmentation in H&E-stained images," *BMC Medical Informatics and Decision Making*, vol. 16, no. 80, 2016, doi: 10.1186/s12911-016-0312-5.
[24] L. He, L. R. Long, S. Antani, and G. R. Thoma, "Histology image analysis for carcinoma detection and grading," *Computer methods and programs in biomedicine*, vol. 107, no. 3, pp. 538-556, 2012, doi: 10.1016/j.cmpb.2011.12.007.
[25] M. Singh, E. M. Kalaw, D. M. Giron, K.-T. Chong, C. L. Tan, and H. K. Lee, "Gland segmentation in prostate histopathological images," *Journal of Medical Imaging*, vol. 4, no. 2, 2017, doi: 10.1117/1.JMI.4.2.027501.
[26] T. T. Tang, J. A. Zawaski, K. N. Francis, A. A. Qutub, and M. W. Gaber, "Image-based classification of tumor type and growth rate using machine learning: a preclinical study," *Scientific Reports*, vol. 9, no. 12529, 2019, doi: 10.1038/s41598-019-48738-5.
[27] T. J. Alhindi, S. Kalra, K. H. Ng, A. Afrin, and H. R. Tizhoosh, "Comparing LBP, HOG and Deep Features for Classification of Histopathology Images," in *2018 International Joint Conference on Neural Networks (IJCNN)*, 2018, pp. 1-7, doi: 10.1109/IJCNN.2018.8489329.
[28] M. Mahdianpari *et al*, "Very Deep Convolutional Neural Networks for Complex Land Cover Mapping Using Multispectral Remote Sensing Imagery," *Remote Sensing*. Vol. 10, no. 7(1119), pp.1-21, 2018, doi: 10.3390/rs10071119.

BIOGRAPHIES OF AUTHORS

Khanabhorn Kawattikul is a full-time lecturer at Department of Information Technology, Faculty of Social Technology, Rajamangala University of Technology Tawan-ok (Chanthaburi Campus), Thailand. He received a master' s degree in information technology from Mahasarakham University, Thailand. The main research of interest is Human-Computer Interaction, Computer Vision, and Machine Learning. His current research falls into a wide variety range of computer vision applications, such as image synthetization. He attempts to generate surreal images of persons from the sketch images. In addition to the information from the image alone, he tries to integrate the information from texts that are used to explain the visual appearance of the faces. He can be contacted at email: khanabhorn_ka@rmutto.ac.th.

Kodchanipa Sermsai is full time lecturer at Department of Information Technology, Faculty of Social Technology, Rajamangala University of Technology Tawan-ok (Chanthaburi Campus). She received a master deegree in Software Engineering from King Mongkut's University of Technology Thonburi, Thailand. The main research of interests in Artificial Intelligence and Machine Learning. She is keen to investigate technique both from handcafted feature-basesd and deep leearning techniques to solve classification problem, especially in computer vision applications. She can be contacted at email: kodchanipa_se@rmutto.ac.th.

Phatthanaphong Chomphuwiset is a full-time lecturer at the Department of Computer Science, Mahasarakham University, Thailand. He received a PhD. in computing from the University of Leeds, UK. His main research interests fall into a variety of areas, including medical image processing, Computer Vision applications, and Machine Learning. One of his current research projects is to investigate techniques in machine learning and deep learning to process histopathological image. He tries to study a computational technique that can cope with the challenge of histopathology image analysis (HIA) where the images pose important challenges such as image size and resolution and the variations of the image–due to the preparation process. He can be contacted at email: phatthanaphong.c@msu.ac.th.