Semi Supervised Grading Model Using Syntactic Level Feature Selection Technique

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Semi supervised grading model using syntactic level feature selection technique

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Abstract Cancer prognosis and the course of treatment chosen are based on the grade of malignancy present as observed in the images. Deep learning approaches have resulted in encouraging outcomes on histopathology images at different levels, such as detection, segmentation, and classification. In this paper, we examine the application of deep learning and image processing techniques to perform automatic breast cancer malignancy grading from histopathology images of Hematoxylin and Eosin (H&E) stains. To determine the grade of malignancy slide, ROI is first extracted from the pre-processed malignant images. From this features were extracted by an intensity level and texture of images, which describe the proportions of nuclei belonging to the various grades, in conjunction with pixel-level feature, and object-level feature. In this study we propose a rough set-based syntactic feature selection method (SFSM)-to create an integrated set of image attributes that can potentially differentiate the varies grades of malignancy image features. Finally, cancer grade was determined by reducing feature vector and classified by the individual Xg-boosting model. Thus, the framework can be clinically used for accurate and rapid diagnosis of breast cancer.

Keywords Breast cancer · Cancer classification · Malignancy grading · Syntactic feature selection · Xg-boosting

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1 Introduction

Cancer is one of the major causes for the existence of an increased mortality rate in the world, and is now one of the major health concerns worldwide. According to the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO), cancer has resulted in the death of about 8.8 million people in 2017. The number of new cancer patients is estimated to be raised annually from 14.1 million in 2012 to 21.6 million by 2030 [15] [1]. Breast cancer is the most common type of cancer among women, and globally about 19.7 million new cases and a mortality rate of 5.8 million women are expected to prevail in the next decade. Histopathology grading of breast cancer is a very important tumour-related indication factor, where both the recurrence and overall survival rate are at their worst expressions in patients with poorly differentiated tumours than the well-differentiated tumours. This grade has an important influence in breast cancer diagnosis and prognosis analysis in clinical practice. It can also provide momentous clinical information about the cancer, and differentiate breast cancer patient sub populations with different type of recurrence risks [23]. Histopathology image is an important area of research for different types of breast cancer in automatic detection. In recent years, cancer grading has become more widely accepted as a powerful indicator of prognosis in detecting breast cancer. The majority of tumour grading systems currently applied to breast cancer combine nuclei grade, tubule size formation and mitotic count. [3] [20].

Barbara et al.[28] compared the performance of co-occurrence, densitometric and morphometric parameters using the automated K-nearest neighbour(Knn) classifier to isolate nuclei from the embedded tissue. Huiting et al. [30] presented a hybrid algorithm with extreme gradient boosting-based weighted k-means algorithm, and evaluated the similarity between two different objects. In [24], authors have presented a digital risk score (DRS) groups by Utilizing tissue micro array (TMA) samples obtained from the primary tumour of patients within a nation wide breast cancer series. DRS classification resulted in a hazard ratio of 2.10 (95% CI 1.333.32, $p=0.001$) for breast cancer survival rate. In recent years, cancer grading has become more widely accepted as a powerful indicator of prognosis in detecting breast cancer. Petushi et al [18] proposed a method automatic breast tumour grading with the density of cell nuclei and the density of tubular cross-sections. Fractal theory is a new area in the field of nonlinear mathematics. Fractal dimension and fractal length are the very important parameters and based on these parameters, texture feature is described. Over the last few years, fractal theory was applied widely in medical image analysis in order to accurately detect cancer cells in the human body because it is so complex and irregular in pattern, and also successfully applied to other sets of images. The important features with similar structures and arbitrarily are presented in a limited scale. [13]. Ran et al [31] developed and validated novel vulnerability biomarkers using fractal geometry features from three-dimensional ultrasound (3D) images. The contributions of the proposed work are briefly explained in the following sections.

The rest of this paper is organized as follows: Section 2 provides the materials and methods. Feature Computation is described in detail in Section 3. Integration based on syntactic rough set theory and Xg boosting model is explained in Section 4.

In Section 5 discussion and results are presented. Finally, the conclusion is given in Section 6.

2 Materials and methods

Breast cancer histological grading fully depends on pathological images, and it is very difficult for professional radiologists to segregate the grades based on histopathology images. Breast cancer grading based on digital histopathology images is a very challenging task, but exploiting the prediction-based model on potential characteristics can benefit diagnosis. In the proposed system features are extracted based on intensity level, densitometric texture, and geometrical features. The syntactic rough set theory is applied in the feature selection model that reduces the features greatly. The features are more comprehensive and useful for classification, which consists of both low-level local details and high-level global syntactic information. Our proposed algorithm mainly consists of four parts: Nuclei detection in malignant image, features computation, syntactic rough set based feature selection, and Xg Boosting model. The overall architecture of the proposed system is represented in figure 1.

Fig. 1 Block diagram of the proposed system

2.1 Nuclei detection

A majority of nuclei methods are based on thresholding techniques. It is well defined for identifying nuclei and there location. The main objective of pre-processing is to enhance the contrast in the input images between the nuclei region and other outer region, which help to extract the boundary accurately. By adopting the method mentioned in [19], we have extracted the ROI of images. Here we performed basic morphological operations; first, the image is converted to binary images and then the morphological operation is performed to extract the boundary of the nuclei image. The pre-processed image corresponds to the boundary of the cell images. The region of interest can be extracted by following the three steps: (1) Detect the topmost non-zero pixel;(2) identify the pixel that belongs to either the rightmost or the left most

region of the nuclei; and (3) locate the nuclei points, namely, X1, X2, X3, X4. This is explained as follows.

It starts from the first column and we search for the binary discontinuity along the rows and columns. We then choose the points that correspond to the very lowest value of the row irrespective of column is R1 and lowest value of column is C1. We carry out this column search by assuming angle rotation of images, which is not more than $\pm 60^\circ$. By extracting the region of interest in the detected malignant image, we can reduce the search area in the whole image, which paves the way for more reliable identification of nuclei and cytoplasm. It also reduces the computation time in finding the nuclei points X1 and X2. In order to identify the region of interest, we first locate the point Rm which is the midpoint between R1 and C1. We then locate the points and obtain a rectangular area to represent the nuclei region from the input images. After the localization of nuclei X1 and X2, the next step is to locate and extract the ROI. Now Rm point traverse perpendicularly towards the nuclei region and let this point be C. Finally, starting from point C, we draw a rectangle of width 90×90 on the nuclei region, which extracts the ROI accurately. The algorithm 1 shows extraction of ROI detection

Algorithm 1: Algorithm for Region of Interest (ROI) extraction

Input : Breast Cancer H&E stain Image

Output: ROI image representing the nuclei images

```

1 begin
2   Extract the outer boundary of the nuclei image using morphological operations;
3   Read filtered image (X);
4   Detect the topmost non-zero pixel;
5   Identify the pixel that belongs to either the rightmost or the left most region of the nuclei;
6   locate the nuclei points, namely, X1,X2,X3,X4;
7   Connect the nuclei points and extract the ROI;
8 end

```

Fig. 2 H&E stained histopathology images: (a), (b), (c), and(d) with different pathological grades and similar representations

3 Feature score computation

In this section we have designed and extracted a total of 220 dimension features from histopathology images. These are intensity, fractal texture and semantic features. They could manage the dependency among pixels, low-level, and high level images, which could be very useful for the image classification [12] [22]. In this work, we propose a adaptive densitometric feature to derive a minimum grey level, maximum grey level, and mean grey intensity level from the extracted ROI. Then geometrical feature is extracted to find out the exact shape and size of the nuclei. For this fractal-based texture feature is measured to evaluate the structure identical complexity of the nuclei. However, the extracted features are based on a clear study of image and human experience. Some features do not help in the discrimination property, so we use the feature selection process to remove useless features from the extracted one. It could bring a reference for the following grade discrimination.

3.1 Feature design and extraction

Grades of breast cancer various from the pathological analysis will be identified in different ways and with different representation in the malignant images. The grey scale value in the reflected region is distributed to pixel intensities in the particular images, which could provide well-defined discriminating and reliable property from the correctly detected nuclei regions in H&E stain images. To reduce the feature dimension, the captured RGB image is initially converted into the grey scale image. The convert function is represented as,

$$Grey = 0.3R + 0.59G + 0.11B \quad (1)$$

where R, G and B are three individual channels for the red, green and blue primary components in the RGB colour space, and grey represents the original grey scale value. Therefore, the converted function is modified as (2) from (1),

$$grey_I = 0.256R + 0.532G + 0.12B \quad (2)$$

where greyI means the modified grey scale value for the proposed algorithm. To further remove the nuclei contour, the enhanced grey scale image with only nuclei corners can be derived by (3),

$$Img(x, y) = grey_I(x, y) + grey_I(x, y - 1) \quad (3)$$

where $Img(x, y)$ is the value of the enhanced grey scale image, x and y are the vertical and horizontal axes in the nuclei region image, respectively. To identify the height and width of the detected ROI, the value is calculated using the following equations,

$$\begin{cases} roi_x[y] = roi_x[y] + 1; \\ roi_x[y] = roi_x[X]; \end{cases} \quad (4)$$

where $roi[x]$ is the projected value onto detected image. From the detected ROI value, the following intensity-level features are extracted. They are Variance (V), Kurtosis (K), Skewness (S), Median (M), Energy (E), Entropy (En), Eccentricity (Ecc) and Centroid (crt).

Fig. 3 (a) Geometrical feature representation, (b) geometric feature based on single nuclei

Adaptive Densitometric feature

The densitometric feature calculated the grey values of the nuclear features from the malignant images that are transformed pixel-wise into densities according to the following formula:

$$AD = \log_{10} \frac{X}{Y} \quad (5)$$

where 'X' is the grey value of the background and 'Y' is the grey value of the pixel nuclei. Based on this evaluation feature, such as, minimum grey value, maximum grey value, mean grey intensity, Kurtosis (K) are extracted [6].

Fractal dimension based texture features(FDTF)

Fractal dimension is one of the important features to measure the roughness texture and complexity of the H&E stain images. Here we consider the image intensity surface as the fractal object are calculated mathematically based on fractal dimension [18][14] [2]. The algorithm computes fractal texture features from the grey Level Co-occurrence Matrix (GLCM). The pattern is distributed based on the entire region of the particular nuclei and measured based on the repetition in the texture. A set of binary images has been obtained from the input grey scale image using the proposed algorithm. In order to describe the segmented texture pattern the fractal dimensions of the resultant regions are computed from each of the binary images. In the proposed FDTF algorithm, the number of decomposed regions has been optimized over the region of interest by estimating the local intensity variation and fractal dimension[9]. The application of the multilevel Otsu's method for the decomposition of the H& E stain image into binary images sometime led to over-segmentation and unnecessary decomposition of the background region of the image[16].

Considering the detected binary image as a binary mask, the region of interest has been extracted from the original grey scale image. It restricted the over-segmentation

and also ensured further decomposition of the grey scale regions from the skin lesion area only, irrespective of the type of surrounding and the nuclei textural pattern of the patient. In the FDTF algorithm the decomposition has been initiated by initializing the decomposition level as the minimum possible grey levels of the image. The masked original grey scale image with initial minimum possible grey levels of the image x_n has been considered to be an input parameter of the algorithm. The multi-level Otsu's algorithm [4][2] has been implemented for the generation of binary images from the input image. The multilevel Otsu's algorithm determines the threshold value that minimizes the input image intra-class variance, considering the grey level distribution of the image, and applies it to each image region until the desired numbers of threshold values, x_n , have been obtained. After obtaining the set of threshold values according to the predefined parameter, the grey scale H&E image is disintegrated into a collection of binary images using two separate approaches. In the first approach, the image is segmented using the set of threshold values individually. In the second approach, a pair of thresholds (lower and upper) is selected and applied to the original grey scale image to get the set of binary image.

Algorithm 2: Algorithm for proposed fractal dimension based texture feature

Input : Breast cancer H& E stain images: 'A' the set of all features, 'B' the set of sequence

Output: 'C' is the reduced feature set

```

1 begin
2   greyI → X
3   Read filtered image (X)
4   For (Each ROI )
5     begin
6       Deduce the indices of all pixels with intensity value;
7       Compute the X- extent and Y- extent of the region to determine the width, height of the
         ROI;
8       Width = max X - minX ;
9       Height = max Y - minY ;
10      Crop ROIε X;
11      Read intensity values of all the pixels of X [row, column]
12    end
13    For each X [row, column]
14      begin
15        Find the pixel with Maximum intensity(MAX);
16        Find the Pixel with Minimum intensity(MIN);
17        Set the MAX and MIN value ;
18      end
19 end

```

$$I_a = \begin{cases} 1, & \text{if } T_l < I(m, n) < T_h \\ 0, & \text{otherwise} \end{cases} \quad (6)$$

where, $I_a(m, n)$ is the resultant binary image T_l and T_h are the selected lower and upper threshold values for original image. For every threshold value various from one

to mean intensity, it update T_l and T_h values. From each of the decomposed regions of the image, after estimating the mean intensity and fractal dimension value the grey scale region is further decomposed. As in Otsu's method the region boundary from each of the resultant binary images is extracted using 8-connected neighbour properties. The algorithm 2 explains fractal dimension based texture feature extraction in the image. Figure3 shows the geometric representation of the feature.

4 Integration based on syntactic rough set theory and Xg boosting model

To improve the classification accuracy and the computation time, we applied the rough set-based features selection and supervised learning models called extreme Gradient Boosting for classification(Xg boosting). We did not simply concatenate these kinds of features into a vector as input to a classifier, such as SVM, RF and so on. This algorithm contains two levels. First, the features will optimize the classifier parameters with the same level of learning ability. We proposed a training model, which could train network again based on the low-level details and high-level syntactic features. The training model makes Xg boosting to take more attention on capturing the high-level syntactic feature to make up extracted features. In training, Xg boosting could update its parameters to overcome the need for extracting corresponding high level features for pathological grades. The inputs of new added flatten layer are the concatenation of selected features and the outputs of average pooling layer of original Xg boosting model with updated parameters. The definition of syntactic rough set-based feature selection is explained based on the following rules as shown in algorithm 3.

Algorithm 3: Algorithm for proposed fractal dimension based texture feature

Input : ' x_k ' the set of all features
Output: ' x_i ' is the reduced feature set

```

1 begin
2   for  $x_i \in x_k$  do
3     if ( $k_i=0$ )
4       set  $x_i$  as Grade 1
5     else if ( $0 < k_i \leq \min_p$ ) then
6       set  $x_i$  as Grade 2
7     else if ( $\min_p < k_i \leq \max_p$ ) then
8       set  $x_i$  as Grade 3
9 end

```

5 Results and discussion

The histopathology H and E stain images of breast cancer is collected. The selected images were obtained by the use of digital photography under the light microscope in

Table 1 Comparison of proposed model with different dataset

Datasets	Method	Precision	Recall	F1-score	Accuracy
TMC	K-NN [27]	0.79	0.735	0.760	0.792
	GoogLeNet [5]	0.902	0.918	0.909	0.903
	ResNet-51 [17]	0.843	0.834	0.839	0.849
	SqueezeNet [29]	0.826	0.915	0.868	0.825
	S-DenseNet [8]	0.939	0.946	0.944	0.954
	Proposed Method	0.971	0.962	0.9661	0.979
BACH-18	K-NN [27]	0.784	0.728	0.759	0.735
	GoogLeNet [5]	0.902	0.924	0.912	0.927
	ResNet-51 [17]	0.847	0.835	0.840	0.837
	SqueezeNet [29]	0.87	0.903	0.887	0.882
	S-DenseNet [8]	0.941	0.944	0.942	0.958
	Proposed Method	0.972	0.959	0.965	0.983
CAMELYON-2017	K-NN [27]	0.79	0.735	0.762	0.783
	GoogLeNet [5]	0.905	0.923	0.913	0.884
	ResNet-51 [17]	0.849	0.835	0.841	0.849
	SqueezeNet [29]	0.82	0.88	0.851	0.874
	S-DenseNet [8]	0.934	0.948	0.940	0.963
	Proposed Method	0.971	0.961	0.964	0.985

Table 2 Digital Hand E stain dataset used in our work

Input Images	Feature Score	Stage Label
Image 1	0.5948	1
Image 2	0.4975	0
Image 3	0.7193	2
Image 4	0.9157	3
Image 5	0.3536	0
Image 6	0.5723	1
Image 7	0.8892	3
Image 8	0.4621	0
Image 9	0.6256	1
Image 10	0.6839	2
Image 11	0.8036	3
Image 12	0.6942	2
Image 13	0.3626	0
Image 14	0.8267	3
Image 15	0.5698	1

2684×1943 size Tagged Image File Format (TIFF) for the BC patient group, which has got ethical approval from the Tata Medical Center (TMC) to carry out this research. Another dataset was collected from the Indiana University Health Pathology Lab. This dataset consists of original data and the corresponding annotations and images of pathological grades.

An overview of our collected H and E stain data is shown in table 3. Table 2 shows the feature score for different stages. We have used a different set of same stain

Table 3 Digital Hand E stain dataset used in our work

Breast cancer grade	Train dataset	Test dataset
Grade 1	234	120
Grade 2	234	120
Grade 3	402	180
Grade 4	402	180

Fig. 4 Average accuracy performance of proposed method and state of the art methods

images. We divided each dataset into the training set and testing set. The detected nuclei regions are extracted and the grey value is standardized into 0 to 255, which is sent to Xg boosting. Training data is extremely insufficient to enlarge the dataset and prevent network over-fitting [26]. All the samples are boosted by scaling, random translation and random rotation. Scaling is set to the proportion of detected nuclei region in the rectangle portion of the network input. At test time, we directly resized the detected nuclei region to 232×232 .

To evaluate the performance of our proposed algorithm, we use quantitative measure, such as classification accuracy (AC). The computation of the metrics are given as:

$$Overall accuracy = \frac{TP + TN}{TP + FN + TN + FP}$$

Here TP denotes the true positive, FP denotes the false positive, TN is the true negative, and FN denotes the false negative. Accuracy means the proportion of true prediction samples in the total classification sample images.

Fig. 5 Performance Evaluation between different datasets

Table 4 Classification performance methods

Model	Accuracy
K-NN[25]	0.703
GoogLeNet[21]	0.74
ResNet-51[10]	0.79
SqueezeNet[11]	0.84
S-DenseNet[7]	0.89
Xgboosting	0.982

Table 5 Ablation studies of Proposed Model

Methods	TCIA		BreakHis		CAMELYON-2017	
	F1-score	DS	F1-score	DS	F1-score	DS
SFSM+SVM	0.862	0.737	0.868	0.737	0.863	0.734
SFSM+CNN	0.925	0.846	0.927	0.842	0.928	0.846
SFSM+XGBoost	0.965	0.883	0.963	0.883	0.966	0.884

5.1 Results based Xg boosting model

To obtain more relevant image features and improve the classification accuracy, selected syntactic rough set features are used as inputs to a Xg boosting model. Generally, the base learning rate is set to 0.001, and is divided by 10 after 50 training epochs. We evaluated the combined network performance on our digital H and E stain image dataset. Comparison is made among various pathological images. The grading sensitivity of features is higher than other algorithms and all the time it gives place at the same false positive rate. It is obvious that feature selection of the syntac-

tic rough set method has a better performance than that of the other methods. That is because of the syntactic rule obtains more information that is hidden in the breast cancer histopathology images and this makes them more useful for cancer grading. We also compared our results with the grading performance of pathological images [26]. Our proposed algorithm has achieved better classification performance with accuracy of 98.67% which is shown in table 4 and in figure ?? . Meanwhile, it also proves the superiority of our proposed algorithm. The best cut-off value of training is 0.381. For this value, we also get a high true positive rate of 0.94 and a low false positive rate of 0.32.

6 Conclusions

In this paper, we proposed to grade breast cancer based on digital H and E stain pathological images, which is non-invasive and convenient. A feature selection algorithm is based on syntactic rough set theory and Xg boosting model. Multi-level features selection by the rough set give more potential information in the H and E stain pathological images and improve the classification accuracy. Our proposed algorithm does not simply feed the features into a classifier that could be trained by the Xg boosting model. We proposed to train the new feature layer network based on the pre-trained grading Xg boosting model to make different parts of the network learn to focus on different levels of features, and this model achieved better performance than other CNN models and had comparative scores with pathological images. In our algorithm, we only considered the features extracted from H and E stain pathological images, and other clinical characters might have an important influence on breast cancer grading. In the future, more newly designed image features and clinical characters are going to be exploited to discriminate breast cancer grades.

Compliance with ethical standards

Conflict of interest: The authors declare that they have no conflict of interest.

Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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