Classification of Prostate Histopathology Images Based on Multifractal Analysis

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SUMMARY Histopathology is a microscopic anatomical study of body tissues and widely used as a cancer diagnosing method. Generally, pathologists examine the structural deviation of cellular and sub-cellular components to diagnose the malignancy of body tissues. These judgments may often subjective to pathologists’ skills and personal experiences. However, computational diagnosis tools may circumvent these limitations and improve the reliability of the diagnosis decisions. This paper proposes a prostate image classification method by extracting textural behavior using multifractal analysis. Fractal geometry is used to describe the complexity of self-similar structures as a non-integer exponent called fractal dimension. Natural complex structures (or images) are not self-similar, thus a single exponent (the fractal dimension) may not be adequate to describe the complexity of such structures. Multifractal analysis technique has been introduced to describe the complexity as a spectrum of fractal dimensions. Based on multifractal computation of digital imaging, we obtain two textural feature descriptors; i) local irregularity: \(f(\alpha)\) and ii) global regularity: \(f(\beta)\). We exploit these multifractal feature descriptors with a texton dictionary based classification model to discriminate cancer/non-cancer tissues of histopathology images of H&E stained prostate biopsy specimens. Moreover, we examine other three feature descriptors; Gabor filter bank, LM filter bank and Haralick features to benchmark the performance of the proposed method. Experiment results indicated that the performance of the proposed multifractal feature descriptor outperforms the other feature descriptors by achieving over 94% of correct classification accuracy.

key words: histopathology, prostate cancer, fractal geometry, multifractal, feature descriptors, classification

1. Introduction

As reported by Globocan 2008[1], prostate cancer is the second most frequently diagnosed cancer of men and fifth most common cancer in overall. Histopathological examination is one of the most reliable methods used for diagnosing prostate cancers. In a histopathological examination, pathologists determine the malignancy of body tissues by identifying the structural deviation of cells or sub-cellular components with respect to their healthy stage. However, these judgments may subjective to the pathologists’ skills and experiences, because of the complexity and diversity of histopathology image texture. Figure 1 shows two prostate histopathology images of cancer and non-cancer regions. In the last two decades, medical diagnosis routines have been partially replaced by Computer Aided Diagnosis (CAD) systems[2]. Particularly, the image analysis based CAD systems observe the structural behavior of the texture or cellular/sub-cellular components using mathematical feature descriptors and discriminate the images according to a quantitative scale.

Various texture feature description methods have been proposed to interpret the texture of medical images, e.g., grey-level co-occurrence matrices[3], wavelet transformations[4], filter banks[5]. Adopting fractal and multifractal analysis to describe the texture is a different approach which is recently being used in the medical imagery research[6]. Fractal and multifractal features describe the behavior of texture from self-similarity viewpoint. This approach has been found to be very effective for describing the tumor architecture in histology images[7],[8].

Histopathology texture often exhibits chaotic and irregular patterns and can be categorized statically into broad class of irregular shaped objects. As a consequence, fractal geometry may appropriately describe the irregular texture patterns of histopathology images. The use of fractal geometry for histopathology images can be found in [9]–[11].

This paper proposes a novel textural feature descriptor based on the fractal geometry. Fractal dimension (FD) of an object is a non-integer exponent, which can be used to describe the complexity of self-similar structure. Multifractal analysis is a generalization of fractal analysis, which aims to describe natural structures (or images) as a speci-
turm of fractal dimensions. Based on the multifractal com-
putation of digital images, one may extract two types of tex-
tural features, i.e., i) local irregularity: $\alpha$ describes the lo-
cal behavior of the pixels associated with its neighbors, and 
ii) global regularity: $f(\alpha)$ describes the distribution of dif-
ferent scales of local irregularities over the entire image. Ad-
ditionally, multifractal computation is subject to a function 
called multifractal measure, which defines a scheme to ob-
serve the dissimilarity of the pixels in a given region. In 
this study, we utilize five multifractal measures to derive 
five-dimensional feature spaces for each $\alpha$ and $f(\alpha)$. The 
multifractal feature space may extract important textural in-
formation, which may not be observable in gray-scale pixel 
domain. Furthermore, we exploit the proposed feature de-
scriptor with texton dictionary based classification model to 
classify prostate histopathology images into cancer and non-
cancer classes.

In this study, the proposed method was experimentally 
evaluated as a classification problem. We classified a set 
of prostate histopathology images into two classes; cancer 
and non-cancer by using three non-parametric classifiers; 
Support Vector Machine (SVM), Random Forest and Ada 
boost. The performance of each classifier was estimated us-
ing different metrics; classification accuracy, sensitivity and 
specificity. Furthermore, we investigated classification per-
formances of other feature extraction methods; Gabor filter 
bank, LM filters (Leung and Malik) [12] and Haralick fea-
tures for the same dataset.

The paper is organized as follows; Sect. 2 reviews dif-
ferent feature extraction methods proposed for medical im-
age classification, Sect. 3 describes the theory behinds the 
fractal and multifractal computations, Sect. 4 illustrates the 
proposed feature descriptor and the classification model, 
Sect. 5 gives implementation details of the experiments and 
analysis of results, and finally Sect. 6 concludes the entire 
work.

2. Related Work

Based on the feature extraction techniques, histopathology 
image classification systems can be categorized into three 
classes; i) Class I extracts the morphological features of cel-
luar or sub-cellular components such as nuclei, lumen and 
cytoplasm. ii) Class II extracts the textural features by using 
a feature descriptor such as filter banks, Haralick operator, 
fractal computation and so on. iii) Class III extracts both 
morphological and textural features. Each method has dif-
ferent advantages and disadvantages. For an example, per-
formance of class I methods is based on the segmentation 
accuracy of desired cellular or sub-cellular components. To 
the contrary, class II methods may overcome that limitation 
by observing the characteristics of the entire texture. How-
ever, they may extract some undesired texture regions such 
as muscles. This section illustrates different feature extrac-
tion methods proposed for medical image classification.

Class III feature extraction algorithm has been pro-
posed for automatic grading of histopathology prostate im-
ages in [13]. They segmented the glandular regions by 
clustering the feature space derived by wavelet transforma-
tion. Both morphological and textural features of glandu-
lar regions have used to classify prostate histopathology im-
ages into five cancer grades. A tree-structured classifica-
tion model has used for the classification. For two prostate 
datasets, the method achieved about 95% and 85% of correct 
classification rates, respectively.

To identify the malignant tissues of prostate images, a 
class III feature extraction method has proposed in [14]. This 
method divided a given region of interest (ROI) of whole 
slide image (WSI) into 100×100 pixels of sub-regions 
and each sub-region is classified into three classes; normal, 
stroma and prostatic carcinoma. They have used Haralick 
operator[15] to extract textural features and segmentation 
results of glands to extract morphological features. They 
evaluated the performance of the system by comparing au-
tomated segmented results with conventional pathologist’s 
annotations. As experimental results shown, 79.3% of sub 
regions of 8 WSIs has been successfully identified.

In [16], a different class III feature extraction method 
has been proposed to discriminate histopathology prostate 
images. This method used three textural features; color his-
togram (16-bins histogram for each color channel of RGB 
color space), fractal dimension [17] and fractal code [18]. 
Morphological features of sub-cellular components such as 
nuclei, cytoplasm, lumen were extracted by using a sys-
tem called MAGIC [19]. They have used Gaussian, $k$-
nearest neighbor and SVM classifiers with sequential for-
ward feature selection algorithm for classifying prostate im-
age dataset. As indicated by the experimental results, this 
method has classified cancer/non-cancer images with 96.7% 
of accuracy and high/low grades of cancer images with 
81.0% of accuracy.

Fractal geometric computation based class II feature 
extracion method was proposed in [11] for grading of 
prostate carcinoma. They used differential box counting 
(DBC) method [20] and entropy-based fractal dimension 
computation method to extract the textural features. Both 
methods involve partitioning the intensity surface into dif-
ferent sizes of grids. They have used four set of different 
grid sizes with each computation method and obtained eight 
dimensional feature space. The proposed feature extrac-
tion method was evaluated by classifying a set of prostate 
histopathology images. This method has obtained around 
94% of correct classification rate for multi-class classifica-
tion of four cancer grades.

Another fractal geometric based class II feature ex-
traction method has been proposed to classify digital mam-
mograms [21]. In their method, a given reference image 
is individually processed by using five image processing 
operators; smoothing operator toward horizontal and ver-
tical directions, threshold operator for high and low in-
tensities and smoothing operator by averaging four neigh-
boring pixels, respectively and obtained six-images includ-
ing non-processed one. They compute FD for each image 
by using differential box counting method and obtained 6-
3. Fractal Fundamentals

Mandelbrot proposed a new geometrical model to describe irregular shape objects, later known as “fractal geometry” [22]. Fractal geometry is based on the idea of self-similar forms. To be self-similar, a shape must be able to be divided into parts, which are more or less similar to the whole. Self-similarity occurs over an infinite range of scales for pure mathematical structures such as Koch’s curve, Cantor set and Sierpinski triangle. However, self-similarity of natural structures is bounded in finite range of scales [23].

In 1984, Pentland showed that intensity surfaces of natural images are partially isotropic fractals. This idea was evolved to describe the roughness of the intensity surfaces of digital images and successfully applied in many digital image processing and medical imaging applications [7], [8], [11], [21], [24]–[26].

3.1 Fractal and Multifractal

Fractal dimension (FD) of an object is a non-integer exponent, which strictly exceed the topological dimension and computed by using the Hausdorff-Besicovitch definition [23].

Let $\Theta$ be a bounded subset of $\mathbb{R}^n$ and $N_{\epsilon}(\Theta)$ be the minimum number of balls of radius $\epsilon$ required to cover $\Theta$. When $\epsilon$ tends to 0, the limiting values of $N_{\epsilon}(\Theta)$ follows the power law $N_{\epsilon}(\Theta) \sim \epsilon^{-d_H}$, where $d_H$ is a constant, i.e., the FD of $\Theta$.

$$d_H(\Theta) = \lim_{\epsilon \to 0^+} \frac{\log(N_{\epsilon}(\Theta))}{\log(\epsilon)} \quad (1)$$

Deterministic structures (mathematically generated by applying the same rule recursively) can be characterized by the same fractal dimension in all scales. In contrast, natural structures are non-deterministic, thus, a single FD may not be adequate to characterize such structures. Multifractal analysis is a generalization of fractal geometrical analysis, which characterizes irregular natural structures as a spectrum of FDs, i.e., multifractal spectrum. Multifractal computation is carried out in two consecutive steps.

At the first step, one may find the local irregularity of a function $\mu$ called “multifractal measure” at a point $x$ of set $S$, as a non-integer exponent, which is described by an H"{o}lder Exponent $h_{\mu}(x)$,

$$h_{\mu}(x) = \lim_{\epsilon \to 0^+} \frac{\log(B(x, \epsilon))}{\log(\epsilon)} \quad (2)$$

where $B(x, \epsilon)$ stands for the closed ball of radius $r$ centered at $x$.

Multifractal analysis of set $S$ consists of computing FD of different size of level sets of $h_{\mu}$,

$$E_h = \{ \mu(h_{\mu}(x) = h) \} \quad (3)$$

where, $E_h$ is a set of points, whose exponents are equal to $h$.

At the second step, one may estimate FD of $E_h$ for different $h$ of $h_{\mu}$ and form a spectrum $d_{\mu}$, i.e., multifractal spectrum of $S$ [27],

$$h \mapsto d_{\mu}(h) = \dim(E_h^\mu), \quad (4)$$

where, $\dim(E_h^\mu)$ stands for the FD of the set $E_h^\mu$.

3.2 Multifractal Analysis on Digital Image

A digital gray scale image can be described by two-dimensional real and non-negative function of gray $g(x,y)$, where $x$ and $y$ are discrete spatial coordinates of the image. Therefore, it is necessary to modify the definitions given in Sect. 3.1 to be appropriate for digital images. It turns out that the limiting value of $\epsilon$ becomes $1^+$ and $B$ becomes a square of side length $\epsilon$ in Eq. (2).

$$h_{\mu}(x,y) = \lim_{\epsilon \to 1^+} \frac{\log(\mu(W_\epsilon(x,y)))}{\log(\epsilon)} \quad (5)$$

where $W_\epsilon(x,y)$ stands for the window of side length $\epsilon$ centered at $(x,y)$.

In the computation, one may plot $\log(\mu(W_\epsilon(x,y)))$ against $\log(\epsilon)$ for $\epsilon = 2i + 1$, $i = 1,2,\ldots$ and estimate the gradient of linear regression line as the local irregularity at point $(x,y)$. Similarly, by computing $h_{\mu}(x,y)$ for every pixel of the reference image, we can derive a matrix of same dimension, which is a feature matrix (or $\alpha$ image).

Subsequently, we quantize the entire range of $\alpha$ (from minimum to maximum) into $R$ discrete sub-ranges. Let $\alpha_r$ be all $\alpha$ values quantized into $r^{th}$ sub-range. $\alpha_r$ may be formed a binary value matrix $I_{\alpha_r}$, which has the same dimension of $\alpha$ matrix.

$$I_{\alpha_r}(x,y) = \begin{cases} 1, & \alpha_{r,\text{Min}} \leq \alpha(x,y) < \alpha_{r,\text{Max}} \\ 0, & \text{otherwise} \end{cases} \quad (6)$$

where, $\alpha_{r,\text{Min}}$ and $\alpha_{r,\text{Max}}$ stand for lower and upper limit of $r^{th}$ sub-range, $\alpha(x,y)$ be the value at point $(x,y)$ in $\alpha$ matrix. Subsequently, it is required to compute FD of each $I_{\alpha_r}$, according to Hausdorff-Besicovitch definition. There
are numerous Hausdorff-Besicovitch dimension computation algorithms and each method has its own theoretical basis to estimate the parameter $N$ in Eq. (1) [6]. Among them, box-counting algorithm is one of the popular FD estimation methods, because of its efficiency, accuracy and easy implementation [28].

To estimate the FD of a binary image $I$, one may cover the entire image using a grid of side length $\varepsilon'$ and count the number of non-empty boxes $N_c(I)$. For digital imaging, $\varepsilon'$ tends to $1^+$. The FD of $I$ is the box-counting dimension $d_B$.

$$d_B(I) = \lim_{\varepsilon' \to 1^+} \frac{\log(N_c(I))}{\log(\varepsilon'^{-1})} \quad (7)$$

Accordingly, one may plot $\log(N_c(I))$ against $\log(\varepsilon'^{-1})$ for $\varepsilon' = 1, 2, \ldots$, and estimate the gradient of linear regression line as the FD of $I$. In this manner, we obtain FD for each $I_n$, and form a multifractal spectrum, which is referred as $f(\alpha)$. Additionally, for each element in the $\alpha$ matrix, we can find a corresponding $f(\alpha)$ values, which leads to a matrix called $f(\alpha)$ (or $f(\alpha)$ image) of the same dimension to the $\alpha$ matrix.

As a consequence, multifractal computation can be utilized to obtain two kinds of textural features; local irregularity: $f(\alpha)$ and global regularity: $f(\alpha)$, respectively.

4. Methodology

The proposed method utilizes the multifractal analysis to describe the texture of histopathology images in a high dimensional feature space. This section illustrates the proposed feature extraction method and its utilization for a texture classification problem.

4.1 Multifractal Feature Descriptor

The textural features presented in $\alpha$ and $f(\alpha)$ are subjective to some multifractal measure $\mu$ (refer Eq. (5)). It turns out that different types of multifractal features can be obtained by appropriately choosing different multifractal measures. In our investigation, we empirically selected five multifractal measures to describe the texture. As a consequence, we obtained five dimensional feature spaces for each $\alpha$ and $f(\alpha)$.

Three multifractal measures; Maximum: $\mu_{\max}$, Minimum: $\mu_{\min}$ and Summation: $\mu_{\sum}$, were selected from [29] and definitions are provided in Eqs. (8a), (8b) and (8c), respectively. We obtain normalized difference in between maximum and minimum intensities of a particular window as a multifractal measure; Ndiff: $\mu_{\text{Ndiff}}$ as shown in Eq. (8d) [30]. These four measures observe the disparity of the gray intensities from four different viewpoints. In addition, gradient operator is widely used to extract the edge information of complex texture. Therefore, we select another measure; Gradient: $\mu_{\text{Grad}}$ proposed in [24] and its definition is given in Eq. (8e), which allow us to analyze the texture through its gradient behavior.

$$\mu_{\max}(m, n) = \max_{(k, l) \in \Omega} g(k, l) \quad (8a)$$

$$\mu_{\min}(m, n) = \min_{(k, l) \in \Omega} g(k, l) \quad (8b)$$

$$\mu_{\sum}(m, n) = \sum_{(k, l) \in \Omega} g(k, l) \quad (8c)$$

$$\mu_{\text{Ndiff}}(m, n) = \left( \frac{\max_{(k, l) \in \Omega} g(k, l) - \min_{(k, l) \in \Omega} g(k, l)}{\varepsilon} \right) \quad (8d)$$

$$\mu_{\text{Grad}}(m, n) = \left( \|G_m\|^2 + \|G_n\|^2 \right)^{1/2} \quad (8e)$$

where $\mu_{(\cdot,m)}(m, n)$ stands for the amount of measure at point $(m, n)$. $\Omega$ is the window of side length $\varepsilon$ centered at point $(m, n)$. $\Omega^c$ represents the non-zero pixels of the $\Omega$. $g(k, l)$ is the gray intensity at point $(k, l)$. $G_m$ and $G_n$ stand for gradient vectors at point $(m, n)$ towards horizontal and vertical directions, respectively.

Furthermore, Fig. 2 shows the appearance of $\alpha$ and $f(\alpha)$ features obtained for the image in Fig. 1 (a), corresponding to each multifractal measure described in Eqs. (8a)–(8e). For finer visualization, we have normalized each image into gray-scale [0, 255].

4.2 Classification Model

In this study, we employed the proposed multifractal feature descriptor with a texton dictionary based classification model to distinguish cancer and non-cancer tissues of prostate histopathology images. Texton dictionary is a collection of distinct texture primitives [31] that can be used to dictate a given texture [32]. When the texture is described in high dimensional feature space, the texton becomes a vector, which has the same dimension to the feature space, the dictionary is a collection of vectors. In addition, the texton dictionary should have an adequate number of distinct textons to describe a given image [12], [33]. More precisely, to obtain high accuracy in the classifier, the texton dictionary should have all possible types of distinct textons of the measured domain. One may construct the texton dictionary by clustering the entire feature-pool, which is derived by using every possible image in the measured domain, and subsequently, find the centroid of each cluster as the element of the dictionary.

In texton dictionary based classification model, the dictionary is used to label all the pixels of an image, which is called texton labeling. One may find the closest texton for each feature vector of the reference image and label each pixel by the corresponding texton’s index. The closest texton is the one, which has minimum Euclidean distance to the given feature vector. Subsequently, one computes a histogram for the labeled image, where each bin represents
the texton’s index (label) and its value indicates the number of occurrences of that label in the entire image. This histogram may be called texture signature of the reference image, because it comprises all characteristics of the image with respect to the utilized feature descriptor.

Subsequently, these texture signatures (feature vectors) are classified by using an appropriate supervised learning classifier. There are two types of supervised learning classifiers; parametric and non-parametric. Parametric classifiers assume that functional forms of the class-conditional distributions are known and non-parametric classifiers make minimal assumptions of class-conditional distributions. The choice of the classifier depends on the sample size and prior knowledge about the class conditional distributions.

5. Experimental Results and Analysis

We examined the performance of the proposed multifractal feature descriptor together with texton dictionary based classification model by classifying a set of prostate histopathology image dataset. This section illustrates; data acquisition, computational parameters of multifractal and other comparative feature descriptors, performance evaluation metrics and the results.

5.1 Data Acquisition

We obtained a sample dataset of H&E (hematoxylin and eosin) stained prostate biopsy specimens of 11 cases. Each sample specimen is scanned as a Whole Slide Image (WSI) of 20x magnification using scanner called Nano-Zoomer. Each WSI can be visualized in eight resolutions such as 1.25x, 2.5x, 5x, 10x, 20x, 40x, 63x, and 100x through a digital slider called NDPViewer. Both Nano-Zoomer and NDPViewer are products of Hamamatsu Photonic K. K.. The approximate size of the WSI at 20x resolution is 33600 × 21000 pixels. The cancer regions of each WSI have been annotated by several experienced pathologists.

The appearances of the components of prostate tissues such as nuclei, cytoplasm, lumen, cell membrane, etc., are slightly varied with the resolution of the WSI. Therefore, pathologists use several resolutions in the digital slider for diagnosing malignant tissues. Moreover, they often use the original resolution (e.g., 20x) or its closer resolutions in the digital slider, because more higher or lower resolution (with respect to the original resolution) images may comprise some visual artifacts. In our experiment, we set up 3 categories of image datasets corresponding to 10x, 20x and 40x resolutions. For each category, by using 11 WSIs, we select 600 sample patches of size 256 × 256 pixels in equal amounts for each cancer and non-cancer regions.

5.2 Multifractal Features Extraction

In our experiment, we compute the \( \alpha \) features according to the definition given in Eq. (5) by setting \( \varepsilon \) as 1, 3, 5, 7, 9, 11, 13. Subsequently, to compute \( f(\alpha) \) features, we quan-
tized α range into 70 discrete sub-ranges and estimated the
FD for each sub-range for \( e' = 1, 2, 4, 6, 8, 10, 12, 14, 16 \) as
defined in Eq. (7). By repeating this procedure for each mul-
tifractal measures described in Eqs. (8a)-(8e), we obtained
5-dimensional \( \alpha \) and \( f(\alpha) \) feature spaces for each image in
the datasets.

5.3 Feature Descriptors for Comparison

The performance of the proposed multifractal feature de-
scriptor is compared with three other widely used feature
descriptors; Gabor filters [34], LM-filters [12] and Haralick
features [15].

Gabor filter bank method is a promising textural feature
extraction technique among existing multi-channel fil-
tering approaches. Gabor filter is generated by modulating
an oriented sinusoidal plane of particular frequency with a
Gaussian envelope. The design of Gabor filter bank is ar-
bbitrary or application oriented. Basically, one may gene-
rate the filter bank by utilizing two parameters; spatial fre-
quency: \( d = 0.25 - 2^{(0.55)/N} \), where \( N \) = image width, and
orientation: \( \theta \) [34]. Our experimental Gabor filter bank was
constructed for \( i = 1, 2, 3, 4, 5 \) and \( \theta = 0°, 45°, 90°, 135° \). As a
consequence, we obtained 20-dimensional feature space to
describe the texture.

LM-filter bank has been successfully applied to recog-
nize the texture of materials made up of both reflectance and
surface normal variations. The LM filter bank consists of 48
filters; first and second derivative of Gaussian filters of 6 ori-
entations and 3 scales making total of 36 filters, 8 Laplacian
of Gaussian filters, and 4 Gaussian filters. LM-filter bank
allows us to describe the texture in 48-dimension of feature
space.

On the other hand, Haralick texture features have been
used in many image understanding applications including
medical and geographical imaging. The calculation of
Haralick features are carried out in two consecutive stages;
i) construction of the co-occurrence matrix and, ii) calcula-
tion of 13 texture features based on the co-occurrence ma-
trix. Two parameters were concerned for constructing co-
occurrence matrix such as scalar distance: \( s \) and orientation:
\( \theta \). In this experiment, we used \( s = 2 \) and \( \theta = 0°, 45°, 90°,
135° \) to compute the co-occurrence matrix. We empirically
decided the value for \( s \) by obtaining maximum correct clas-
sification rate for 20x resolution image dataset with SVM.
Subsequently, we computed the features; Angular Second
Moment, Contrast, Correlation, Sum of Squares: Variation,
Inverse Difference Moment, Sum Average, Sum Variance,
Sum Entropy, Entropy, Difference Variance, Difference En-
tropy, Information Measure of Correlation 1 and Correlation
2, for each co-occurrence matrix. As a consequence, we ob-
tained 52-dimensional feature space to characterize a given
image.

5.4 Classification

We utilized \( k \)-means clustering with \( k = 300 \) to construct
texton dictionaries for feature descriptors; \( \alpha, f(\alpha) \), Gabor
and LM. We empirically decided that 300 textons are ade-
quate to obtain optimal correct classification rate. As a
consequence, \( \alpha, f(\alpha) \), Gabor and LM feature sets use 300
dimension of feature vector (histogram of 300 bins) to char-
acterize the texture of a given image. Haralick feature de-
scriptor uses 52-dimension feature vector. Subsequently, we
utilized these feature vectors with three supervised learning
non-parametric classifiers: SVM [35], Ada Boosting [36]
and Random Forest [37] to perform two-class classification;
cancer and non-cancer. As the implementations of the clas-
sifiers we used MatLab SVM toolbox [38], GML AdaBoost
Matlab Toolbox [39] and Randomforest-Matlab [40].

5.5 Performance Estimation

Typical supervised learning based classification systems
have two stages; i) learning: the classifier learns the sys-
tem parameters, ii) testing: the classifier makes prediction
to evaluate the performance of the system. For a small sam-
ple set, \( k \)-fold cross validation is one of the popular popu-
lar strategy used to reduce bias of the classifier in machine learning
and testing [41]. In our experiment, 10-fold cross validation
is performed, namely, in every iteration 540 samples were
selected for learning and 60 samples were used for testing.

We used several statistical error estimation metrics to
calculate the performance of feature descriptors. The met-
ic of correct classification rate CCR is estimated as CCR =
\( n_c/n \), where \( n_c \) denotes the number of correctly classified
samples and \( n \) is the total number of samples used for test-
ing. Additionally, the predictions of a binary class classifi-
cation diagnostic system derives a confusion matrix of four
possible parameters; i) True Positive (TP), ii) True Neg-
ative (TN), iii) False Positive (FP) and iv) False Negative
(FN). We computed two statistical measures; Sensitivity
and Specificity from the confusion matrix as
\[
sensitivity = TP/(TP+FN) \quad \text{and} \quad specificity = TN/(FP+TN)
\]
More pre-
cisely, sensitivity measures the proportion of correctly iden-
tified actual positives and specificity measures the propor-
tion of correctly identified actual negatives. The diagnostic
systems aim to achieve 100% for both sensitivity and spec-
ificity. The averages of CCR, sensitivity and specificity in
each iteration of the cross-validation were taken to examine
the performance of the classification.

5.6 Results and Discussion

We examined the classification performance through CCR,
sensitivity and specificity as shown in Tables 1 and 2. Ta-
ble 1 has categorized the results as classifier, resolution
(magnification scale) of the dataset and feature descriptor.
Table 2 presents the average performance of each feature de-
scriptor of all three resolutions of image datasets. We have
used the format \( x \pm y \) to present the CCR, where \( x \) and \( y \) are
sample mean and standard error for 95% confidence interval
respectively.

It is apparent from Table 1 that for every resolution
of image dataset, multifractal features have obtained significant performance for each quality measure compared to the other feature descriptors. Table 2 also concludes that $\alpha$ and $f(\alpha)$ features outperformed other features descriptors irrespective to the magnification of the images. Particularly, Table 2 showed that $\alpha$ and $f(\alpha)$ features have obtained 94.63% and 94.59% of CCR, 91.23% and 92.00% of sensitivity, 90.00% and 91.00 of specificity, respectively with SVM classifier. As a overall summary, both $\alpha$ and $f(\alpha)$ features have obtained over 94% of CCR and over 90% of sensitivity and specificity. It turns out that fractal geometry appropriately describes the complex texture patterns in prostate histopathology images.

We note here that, feature descriptors $\alpha$, $f(\alpha)$, Gabor and LM have used 300 dimension of feature vectors; to the contrary, Haralick features consisted of 52 dimension of feature vectors. Even though, higher dimension of feature vectors increase the computational cost of the classifier, higher accuracy is anticipated in medical diagnosis systems.

6. Conclusion

Typical histopathological judgments may be subjective and often lead to have considerable variation. To circumvent this issue and improve the reliability of cancer diagnosis, it is important to develop computational tools for classifying histopathologic images that operate on quantitative measures. This paper proposed a new feature descriptor to characterize the texture based on fractal geometry. By using five multifractal measures, we computed two types of multifractal descriptors: $\alpha$ and $f(\alpha)$, which provide local irregularity and global regularity information of the texture, respectively. We employed the proposed feature extraction method with textron dictionary based classification model to discriminate a set of images of H&E stained prostate biopsy specimens into cancer and non-cancer classes. Three types of supervised learning classifiers were used, SVM, Random Forest and Ada boost. The performance of each classifier was estimated through three statistical measures; correct classification rate, sensitivity and specificity. Furthermore, the merit of the proposed method was examined by comparing the performance of the proposed method with three textural feature descriptors; Gabor, LM and Haralick. Experimental results indicated that the proposed feature descriptor outperformed the other feature descriptors.

Furthermore, the proposed feature descriptor is independent of the computation of morphological characteristics of tissue level component such as nuclei. Instead, it observes the entire textural information. Therefore, the proposed feature descriptor may be useful for discriminating cancerous

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**Table 1** Classification results for SVM, RandomForest and AdaBoosting classifier.

| Resolution | Feature | CCR (%) | Sensitivity (%) | Specificity (%) |
|------------|---------|---------|----------------|----------------|
| 10x        | $\alpha$ | 95.80±3.66 | 91.00 / 90.50 | |
|            | $f(\alpha)$ | 95.20±4.29 | 92.00 / 91.50 | |
|            | Gabor     | 84.00±4.39 | 88.67 / 79.33 | |
|            | LM        | 82.17±3.85 | 86.67 / 77.67 | |
|            | Haralick  | 83.00±7.53 | 83.33 / 77.67 | |

**Table 2** Average classification performance of each feature.

| Feature | Classifier | CCR (%) | Sensitivity (%) | Specificity (%) |
|---------|------------|---------|----------------|----------------|
| $\alpha$ | SVM        | 94.63±3.86 | 91.23 / 90.00 | |
|         | RandomForest | 91.85±4.86 | 92.50 / 87.00 | |
|         | AdaBoost   | 91.00±5.74 | 84.67 / 80.97 | |
| $f(\alpha)$ | SVM        | 94.59±4.76 | 92.00 / 91.00 | |
|         | RandomForest | 91.83±6.09 | 89.33 / 86.27 | |
|         | AdaBoost   | 89.50±9.05 | 80.83 / 71.73 | |
| Gabor   | SVM        | 81.91±5.20 | 80.56 / 75.00 | |
|         | RandomForest | 79.28±4.72 | 76.22 / 82.33 | |
|         | AdaBoost   | 68.22±7.20 | 76.56 / 56.55 | |
| LM      | SVM        | 81.83±5.58 | 82.89 / 77.44 | |
|         | RandomForest | 81.11±4.43 | 78.00 / 84.22 | |
|         | AdaBoost   | 77.28±8.04 | 79.11 / 65.44 | |
| Haralick | SVM       | 83.67±5.79 | 87.78 / 77.56 | |
|         | RandomForest | 84.22±3.80 | 85.89 / 82.56 | |
|         | AdaBoost   | 81.61±5.78 | 84.00 / 79.22 | |
tissues or their grades of other body organs.

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