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Cell phenotype classification using multi threshold uniform local ternary patterns in fluorescence microscope images

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Abstract

Identifying locations of protein expression in live cells plays an important role in several medical applications ranging from early disease diagnosis to monitoring effectiveness of drugs. Protein localization is directly related to their cell types. Today florescence imaging is widely used to understand biology at the cellular level. Hence, cell phenotype classification in fluorescence microscope images, is related with protein localization. Today it is performed by human, which is very time consuming with low accuracy. According to the visual structure, it can be seen that samples of a unique cell type have quite similar texture, but the texture of different cell types, are very different. In this respect, texture information can be used more widely than shape or color information, to classify types. Local ternary pattern is a noise-resistant texture descriptor that provides discriminative features. In this paper a local texture analysis descriptor is proposed titled multi threshold uniform-based local ternary patterns with notation MT-ULTP. MT-ULTP extracts local significant texture information in different locality levels. In this respect, local ternary patterns are extracted in different thresholds and finally the occurrence probability of the uniform patterns is extracted as features. MT-ULTP is a skillful combination of LTP and MLBP with novelty in feature extracting and local pattern selecting. Performance of the proposed descriptor is evaluated on 2d-hela dataset in terms of accuracy. 2d-hela is the benchmark dataset of cell phenotype images. Experimental results show that MT-ULTP provides higher classification rates than very well-known texture descriptors such as lbp-like descriptors. In other experiments, it has been shown that ignoring uniform textural patterns in the image analysis can increase the accuracy of cell phenotype classification and some other computer vision-based applications. The results also showed that extraction uniform patterns based on a combination of thresholds provide better results than the simple form in local ternary patterns. The proposed image texture descriptor is a general case which can be used in many computer vision applications to describe the image contents.

Keywords

Cell phenotype classification, Fluorescence microscope images, Feature extraction, Texture image analysis, Multi threshold uniform local ternary patterns

1. Introduction

Identifying the locations of protein expression in live cells plays an important role in biological sciences. Protein localization is a critical task in several medical applications ranging from design of drug screening systems to early cancer diagnosis. Today florescence imaging is widely used as an effective tool to understand biological features of cells by means of visualization. Hence, cell phenotype classification in fluorescence microscope images, is deeply related with protein localization. It is performed today by expert humans. It is very time consuming task with low accuracy in some situations. In recent years various methods have been proposed for automatic cell phenotype classifications. Most of them work based on computer vision and machine learning techniques. This task is categorized as an offline problem because of its relation with patient's life. Therefore, in almost all the methods presented so far, the main aim is to increase the classification accuracy of the system. Most of vision-based methods follow the same strategy that involves two main steps of feature extraction and classification. In most ways, researchers have attempted to extract features that, firstly, have high discrimination power and, secondly, can be a good representation of the image content. For this reason, most researchers are attempting to analyze the ability of common feature extraction operators to classify cell phenotypes. Some examples of 10 different popular cell phenotypes are shown in figure 1.

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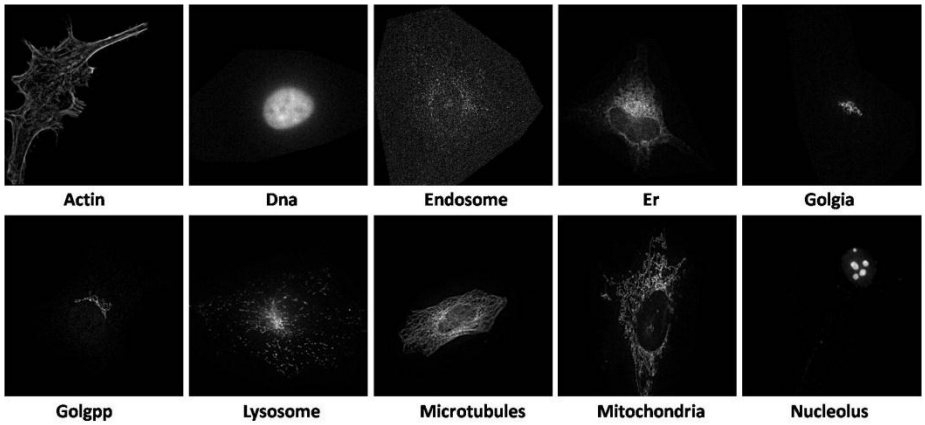

Figure 1. Some examples of cell phenotype images in ten classes

For example, a combination of global and local operators, such as wavelets, local binary patterns, threshold statics, haralick and edge features, has been used to classify cell phenotypes [1]. Also, random subspace of Levenberg–Marquardt neural networks has been used for the classification step [1]. An optimal subset of statistical shape, geometric and texture features is used in [2] in relation with a two-layer back propagation neural network (BPNN) for protein localizations. Various types of lbp-like family descriptors have been used in [3] to extract discriminative features of phenotype cell fluorescence images. As the classifier, a stand-alone support vector machine (SVM) and a random subspace ensemble of SVM are used in [3]. Numerous other articles have addressed this issue with a same strategy, where, some of them are discussed in section 2 with details.

In this paper, a different motivation is followed for cell phenotype classification. Our main contribution in this paper is as follows:

Popular image descriptors may not alone be efficient for cell phenotype classification. So, current efficient descriptors should be modified with respect to the unique appearance characteristics of cells and fluorescence microscopic imaging conditions. In this respect two main goals are following in this paper:

- Increase the classification accuracy rate of cell phenotype images analysis, in comparison with state-of-the-art methods in this scope.
- Define a modified image texture descriptor with better results than common descriptors for cell phenotype classification.

In this respect, a modified image texture descriptor is proposed titled multi threshold uniform local ternary patterns with notation MT-ULTP. This operator is an improved version of the local ternary patterns (LTP) that has defined based on two following contributions:

- Consideration of local non-uniform patterns in the feature extraction stage reduces the classification accuracy of the cell phenotype classification.
- The combination of features derived from applying different local thresholds provides better results than using a unique local threshold in processing of LTP.

2. Recent works

Various methods have been proposed to classify cell phenotype images. The main difference in methods is in the feature extraction or classification phase. This section discusses some of the effective methods in this field. In all methods, researchers have attempted to use common image descriptors for feature extraction or adjust their input parameters to increase the accuracy. Articles don't usually attempt to improve common image texture descriptors based on the unique properties of cell phenotypes or the fluorescence microscope imaging properties.

Nanni et al. [1], proposed an approach for automatic cell phenotype image classification with the aim of protein localization. Nanni et al., in [1] concentrated on designing a set of optimal features and then applying best classification algorithm. In this respect a combination of global and local descriptors such as invariant local binary patterns (ILBP), threshold adjacency statics, Haralick features, edge and wavelet are used for feature extraction. Next, they focused on the study of ensemble machine learning techniques for cell phenotype image classification. Two techniques are tested in [1] for the classification stage: a random subspace of Levenberg–Marquardt neural networks and a variant of the AdaBoost. The number of used feature extractors in [1] is more than some well known methods in this scope. Also, ensemble methods usually have higher complexity in comparison with unique classifiers. So, high computational complexity can be considered as one of the main disadvantages of [1].

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Murphy et al., [2] designed a set of numeric features for sub cellular location classification, which are robust to intensity binning and spatial resolution. The types of feature used in [2] are Haralick texture features, Zernike moment features, features derived from morphological operations, features derived from comparison with a reference image of the DNA distribution. The feature set had been evaluated using several classification methods. Finally, two-hidden-layer BPNNs provides best results for the 2D HeLa dataset.
Deep neural networks have become one of the benchmark methods for biomedical image classification. In many cases, transfer learning using convolutional neural networks (CNN) is applied to obtain high classification accuracy. Nguyen et al., [4] proposed a deep neural network architecture based on transfer learning for fluorescence microscopic image classification. In [4], first, some features extracted from three pre-trained deep CNNs are concatenated. Then, two fully-connected layers of CNN are trained based on extracted features. Experimental results of [4], shows that their proposed network architecture produces significant performance gains in comparison with neural network structures that uses only features extracted from single CNN.
Nanni et al., [5] is focused on the study of texture descriptors for training an ensemble of machine learning algorithms for cell phenotype image classification. Nanni et al., [5] proposed a new approach based on a fusion of Levenberg–Marquardt neural networks, which are trained by a random subspace of global and local features. In order to provide the optimum set of features some benchmark descriptors such as spatial gray level dependence matrices (SGLD), local ternary patterns and local binary patterns are used.
In [6], Xuantao et al., proposed a visual cyometric pattern recognition algorithm for unsupervised cell classification. in [6], single cell images are captured using two dimensional (2D) light scattering cytometer. Adaptive boosting (AdaBoost) algorithm is adopted for the analysis of the 2D light patterns. Xuantao et al., demonstrated that the pattern recognition cytometry can perform unspervised classification of normal cervical cells and HeLa cells with high accuracy.
Lin et al., [7] proposed an algorithm to analyze microscopic images based on the bag-of words (BoW) and the softmax regression. Lin et al., [7] used the locality-constrained linear coding (LLC) to extract local texture features because the LLC encodes local structures of microscopic images with lower quantization errors. Linear softmax regression classifier is then used to classify cell types. Experiment results on the 2DHela data sets [8], show significant performance improvement of their algorithm comparing with non linear classifiers.

3. Fundamentals

The main purpose of this paper is to present a method for cell phenotype classification. This problem is categorized as visual pattern recognition problems. Therefore, it consists of two main steps, feature extraction and classification. As mentioned, the phenotype microscopic structure of cell types is highly similar in color and shape. But the expertise of the experts shows that different cell types are different in texture. Therefore, an texture image descriptor with high discriminative power is needed during feature extraction. In this respect, a descriptor is proposed in this paper as multi threshold uniform-based local ternary patterns with notation MT-ULTP. MT-ULTP is a lbp-like family descriptors with higher discrimination power in comparison with other family members such as LBP, MLBP and LTP.

3.1. Local binary patterns (LBP)

LBP is a simple, powerful and non-parametric texture descriptor that extracts local spatial structure and local contrast information [9]. The main contribution in LBP is considering local texture information in different resolution degrees. To process LBP, first a symmetric neighborhood is considered for each pixel. Mostly circular neighborhood is chosen to achieve rotation invariant. Some examples of circular symmetric neighborhoods in different radius (R) and number of neighbors (P) is shown in figure 2. Next the LBP value for each neighborhood is extracted using difference value between center and its neighborhoods, expressed by Eq.1.

$$LBP_{P,R} = \sum_{i=0}^{P-1} S(g_i - g_c)2^i \qquad (1)$$

Where R is the radius of neighborhoods and P is the number of neighboring points. g_c denotes the intensity value of the central pixel and g_i is the intensity value of neighboring. The step function of s(x) is defined by Eq.2.

$$s(x) = \begin{cases} 1 & if\ x \geq 0 \\ 0 & otherwise \end{cases} \qquad (2)$$

$LBP_{P,R}$ extracts a binary code with P-bits for each pixel with 2^P different values. The binary code is converted to a decimal number. When image is rotated, the gray values g_i will correspondingly move along the perimeter of the circle around g_c. In order to assign a unique value, the minimum value of rotated neighborhoods is selected based on Eq.3.

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$$LBP_{P,R}^{ri} = \min\{RoR(LBP_{P,R}, i \mid i = 1, \dots, P \quad (3)$$

Where *ri* denotes the rotation invariant and ROR($LBP_{P,R}$,i) rotates the local binary pattern circularly to the right *i* times and the minimum value for i=0 to P-1is selected. By applying LBP operator to an image, each pixel of the image is labeled between 0 to 2^P-1.

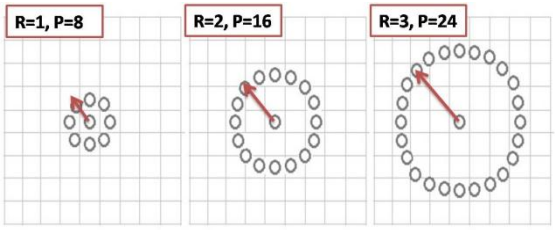

Figure 2. Circular symmetric neighborhoods in different radius used in LBP process

3.2. Local Ternary Patterns (LTP)

Impulse noise sensitivity is one of the main disadvantages of basic LBP. Since now, many LBP versions have been proposed to solve this problem such as hybrid color local binary patterns (HCLBP) [10], local ternary patterns (LTP) [11] and noise resistant local binary patterns (NRLBP) [12]. LTP is a simple and general texture descriptor which can be used in many cases to extract image texture information. LTP extracts a ternary code for each neighbourhood, which is a 3-valued code (-1, 0, 1). The LTPs is defined as follows:

$$\mathrm{LTP}_{P,R} = \sum_{i=0}^{P-1} s(g_i - g_c)3^i \quad , \quad \text{Where} \quad s(x) = \begin{cases} 1 & if \quad x \geq BT \\ 0 & if \quad |x| < BT \\ -1 & if \quad x \leq BT \end{cases} \quad (4)$$

Where, *BT* known as binarization threshold. *BT* describes the significant amount of local differences between center and neighbors. Output of the $LTP_{P,R}$ operator for each pixel of the image is a P-bit binary number with 3^P different values. 3p different values increase the total number of extracted features and finally computational complexity. In order to decrease complexity, the ternary code is divided into two upper and lower binary patterns. An example of LTP encoding procedure and split it into upper and lower patterns is illustrated in figure (3).

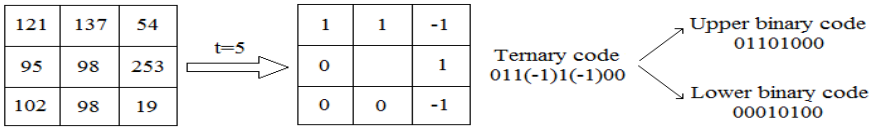

Figure 3. An example of LTP encoding procedure and its upper and lower patterns

4. Proposed cell phenotype classification approach

4.1. Proposed Multi Threshold Uniform-based Local Ternary Patterns (MT-ULTP)

Noise sensitivity of LTP is lower than many other lbp-like approaches. But, the runtime of LTP is high and with increasing number of neighboring points, this complexity increases. Also, the discriminate power of the histogram features extracted from LTP is not enough in many computer vision applications such as pap smear image classification [13]. As noted, the main motivation of this research is to provide a texture image descriptor which is optimized based on the cell phenotype properties. In this regard, the following two observations are followed in the proposed modified texture descriptor (MT-ULTP).

Observation #1. As can be seen in Fig. 1, due to the properties of fluorescence microscope imaging, the organs around the cells do not contain texture information. Also, there are not many local differences in terms of intensity, in these parts. Therefore, extracting non-uniform patterns is not necessary and only increases the computational complexity.

Observation #2. The structure of cell samples of a same class is very similar in texture, but their phenotype power are not the same in terms of illumination. In some cases local differences between pixel intensities is lower than many other parts. Therefore, the use of fixed-threshold for texture analysis descriptors cannot be efficient.

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Ojala et al., [18] proposed a new feature extraction based on LBP which is notified by MLBP. In MLBP process, a uniformity measure U, which represents the number of spatial transition (bitwise 0/1 changes) in the binary pattern, is defined to categorize extracted local binary patterns. It is shown in Eq.5. For example, U value in 10000111 pattern is 2 while U value in 00000000 and 11111111 patterns is 0.

$$U(LBP_{P,R}) = | s(g_{P-1} - g_c) - s(g_0 - g_c) | + \sum_{P=1}^{P} | s(g_P - g_c) - s(g_{P-1} - g_c) | \quad (5)$$

Next, the patterns that have U value less than U_T are defined as uniform patterns and the patterns have U value more than U_T are defined as non-uniform patterns. In many cases, this feature extraction schema (uniform based) provided better results than histogram analysis of lbp-like descriptors.
In our proposed MT-ULTP descriptor, this feature extraction schema is extended to basic LTP as follows to achieve more discriminative feature set:

a) The LTP process is done for each local neighborhood. Next, uniformity measure is computed for upper and lower LTP individually.
b) Upper patterns categorized in two groups (uniform and non-uniform) based on U_{UT} (Eq. 6)
c) Lower patterns categorized in two groups (uniform and non-uniform) based on U_{LT} (Eq. 7)
d) Based on the Observation #1, all patterns that are identified as non-uniform will be ignored in the computation and will not be labeled.
e) For each uniform local neighborhood, a label is assigned to upper extracted pattern (Eq. 8)
f) For each uniform local neighborhood, a label is assigned to lower extracted pattern (Eq. 9)
g) Occurrence probability of labels can be considered as features. So, one feature vectors for upper patterns and lower patterns can be extracted with 2×(P+1) dimensions separately. (Eq. 10-11).
h) Based on observation #2, the appearance of cells in a same class is usually not constant. Therefore, features should be extracted with different power in relation with binarization threshold. Finally, all the upper and lower feature vectors at all binarization thresholds, should be concatenated to provide final feature vector.(Eq. 12)

$$UG_U(x,y) = \begin{cases} Uniform & if\ U\left(ULTP_{P,R}(x,y)\right) < U_{UT} \\ Non-Unifrom & else \end{cases} \quad (6)$$

$$UG_L(x,y) = \begin{cases} Uniform & if\ U\left(LLTP_{P,R}(x,y)\right) < U_{LT} \\ Non-Unifrom & else \end{cases} \quad (7)$$

Where, U_{UT} is the uniformity threshold to categorize uniform and non-uniform patterns between upper binary extracted patterns. Where, U_{LT} is the uniformity threshold to categorize uniform and non-uniform patterns between lower binary extracted patterns. Also, UG_U and UG_L show the uniformity group of upper and lower neighborhoods in coordinates (x,y).

$$Label\ (U-ULTP^{riu_T}_{P,R,BTi}(x,y)) = \sum_{k=1}^{P} |S(g_k - g_c)| \quad if\ \ UG_U(x,y) = uniform \quad (8)$$

$$Label\ (L-ULTP^{riu_T}_{P,R,BTi}(x,y)) = \sum_{k=1}^{P} |S(g_k - g_c)| \quad if\ \ UG_L(x,y) = uniform \quad (9)$$

$$F^{BTi}_{U-ULTP} = \{f_0, f_1, \dots, f_p,\} \quad \text{Where} \quad f_k = \frac{N_{Uk}}{N_{total}} \quad (10)$$

$$F^{BTi}_{L-ULTP} = \{f_0, f_1, \dots, f_p,\} \quad \text{Where} \quad f_k = \frac{N_{Lk}}{N_{total}} \quad (11)$$

Where, F^{BTi}_{U-ULTP} means the extracted feature vector for upper uniform patterns using LTP and binarization threshold *BTi* in coordinates (x,y). Where, F^{BTi}_{L-ULTP} shows the extracted feature vector for lower uniform patterns using LTP and binarization threshold BTi in coordinates (x,y). Also, the f_i is the occurrence probability of i^{th} label in whole images. N_{Uk} is the number of local neighborhoods with label k in upper patterns. N_{Lk} is the number of local neighborhoods with label k in lower patterns. N_{total} is the total number of local neighborhoods in the images.

$$F_{MT-ULTP} = \{F^{BT1}_{U-ULTP}, F^{BT1}_{L-ULTP}, \dots, F^{BTi}_{U-ULTP}, F^{BTi}_{L-ULTP}, \dots, F^{BTn}_{U-ULTP}, F^{BTn}_{L-ULTP}\} \quad (12)$$

BT_i shows the ith binarization threshold, where n is the total number of used thresholds. $F_{MT\text{-}ULTP}$ is the final extracted feature vector. As can be seen in Eq. 12, the total number of dimensions in the final vector is directly related with the number of used binarization thresholds and neighborhood radius (R). For example, if three different value is considered as BT, finally 54 features is provided using $LTP_{8,1.}$ Because all of the non-uniform patterns are omitted in the process, these patterns should cover a small portion of the patterns in texture, In [14], it is showed that if value of uniformity threshold (U_{UT} and U_{UT}) is selected equal to P/4, only a small portion of the patterns in texture takes label non-uniform.

5. Results

To evaluate the performance of the proposed cell phenotype classification approach, all experiments carried out on benchmark cell phenotype datasets: 2d-Hela [15]. The properties of 2d-Hela dataset samples are shown in table 1. Computer specifications to evaluate the performance of proposed approach are shown in table 2.

Table 1. Properties of the benchmark 2d-Hela datasets used in experiments

Dataset properties	2D-Hela
Sample numbers	862
Class numbers	10
Number of class samples	Different about 73-98
Image size	382 × 382
Format	TIFF
Horizontal resolution	72 dpi
Vertical resolution	72 dpi
Bit depth	16
Illumination shadow	No
Scale Change	Yes

Table 2. Computer specifications used in experiments

Computer properties	Specifications
CPU	Intel Core2Duo
Core	2 cores (2.10 GHz)
RAM	4.00 GB
Simulation	MATLAB (R2010-B)
Operating System	64 bit

5.1. Evaluation results of the observation #1

The main aim of this paper is to propose a new method for cell phenotype image classification. In this respect a set of numeric features are extracted based on proposed MT-ULTP. The proposed features are general so each numerical classifier can be used here to evaluate the performance. In this respect, some different classifiers (Baysian network, Multi layer perceptron, J48 Tree, random forest and KNN) are employed in this experiment to achieve classification accuracy. The number of used binarization thresholds and the radius of local neighborhoods are variable in the proposed method, which make it useful in many computer vision applications. So, these experiments are evaluated based on different values. In all experiments, 10-folds algorithm is used as cross validation method.

Two theories are followed in this paper to describe MT-ULTP. The first observation is about omitting the non-uniform patterns in the feature extraction process. In this respect, an experiment is designed to evaluate the performance of the observation #1. The cell phenotype classification is done based on basic LTP and proposed MT-ULTP. The results are shown in the table 3. As can be seen, the maximum accuracy is provided using MT-$ULTP_{8,1}$ in single descriptor without any combination. Also, in combination manner, LTP81,+LTP16,2 provided maximum accuracy about 86.77 percent which is more than combination of MT-ULTP8,1+MT-ULTP16,2 about 0.23 percent which is not significant difference. Each row in colored blocks shows a unique pair-comparison between proposed MT-ULTP and LTP in different terms such as binarization threshold (BT) and neighborhood radius (R). In more than 71 percent of the pair experiments, MT-ULTP provide better or same results in comparison with basic LTP in different classifiers and binarization thresholds.

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Table 3. Classification accuracy (%) using MT-ULTP and LTP on 2d-Hela

Descriptor / Classifier	$MT\text{-}ULTP_{8,1}$	$LTP_{8,1}$	$MT\text{-}ULTP_{8,1} + MT\text{-}ULTP_{16,2}$	$LTP_{8,1} + LTP_{16,2}$	Binarization threshold
Bayesian network	59.39	59.97	62.87	62.64	BT_1=2, BT_2=5, BT_3=8
J48 Tree	70.53	73.43	71.46	72.62	BT_1=2, BT_2=5, BT_3=8
Random forest	83.52	84.45	86.42	85.96	BT_1=2, BT_2=5, BT_3=8
MLP	84.91	82.94	60.44	56.61	BT_1=2, BT_2=5, BT_3=8
1-NN	82.48	82.94	85.73	86.65	BT_1=2, BT_2=5, BT_3=8
3-NN	80.85	80.85	86.19	**86.77**	BT_1=2, BT_2=5, BT_3=8
5-NN	80.39	80.85	86.54	85.84	BT_1=2, BT_2=5, BT_3=8
Bayesian network	52.55	52.55	60.09	59.86	BT_1=2
J48 Tree	66.47	66.47	70.64	70.18	BT_1=2
Random forest	78.07	77.49	83.64	83.41	BT_1=2
MLP	78.42	77.61	82.01	80.62	BT_1=2
1-NN	75.87	75.87	83.75	83.87	BT_1=2
3-NN	75.05	75.05	83.87	84.22	BT_1=2
5-NN	75.75	75.75	83.75	83.52	BT_1=2

5.2. Evaluation results of the observation #2

The second observation is about using multi binarization thresholds for applying ULTP. In this respect, an experiment is designed here to evaluate the performance of the observation #2. The cell phenotype classification is done based on different thresholds. Firstly, it is done based on one static binarization threshold. Next it is repeated using two and three binarization thresholds. The results are shown in the table 4.

Table 4. Classification accuracy (%) using MT-ULTP with different binarization threshold value on 2d-Hela

Classifier / Operator	binarization thresholds	Bayesian Network	Naïve Bayes	J48 Tree	Random Forest	MLP	1-NN	3-NN	5-NN
$ULTP_{8,1}$	BT_1=2	52.55	42.45	66.47	78.07	78.42	75.87	75.05	75.75
$MT\text{-}ULTP_{8,1}$	BT_1=2, BT_2=5	51.85	43.61	68.90	80.51	84.10	77.49	76.91	75.52
$MT\text{-}ULTP_{8,1}$	BT_1=2, BT_2=5, BT_3=8	59.39	46.40	70.53	83.52	84.91	82.48	80.85	80.39
$ULTP_{16,2}$	BT_1=2	57.19	51.85	66.35	78.30	78.07	78.88	79.93	80.97
$MT\text{-}ULTP_{16,2}$	BT_1=2, BT_2=5	60.90	53.59	69.72	84.33	84.08	82.13	82.71	83.41
$MT\text{-}ULTP_{16,2}$	BT_1=2, BT_2=5, BT_3=8	61.48	55.56	68.09	83.41	83.16	83.64	83.75	82.71
$ULTP_{8,1} + ULTP_{16,2}$	BT_1=2	60.09	51.16	70.64	83.64	82.01	83.75	83.87	83.75
$MT\text{-}ULTP_{8,1} + MT\text{-}ULTP_{16,2}$	BT_1=2, BT_2=5	60.55	51.97	72.38	86.07	69.60	84.22	85.03	84.45
$MT\text{-}ULTP_{8,1} + MT\text{-}ULTP_{16,2}$	BT_1=2, BT_2=5, BT_3=8	62.87	54.75	71.46	**86.77**	60.44	85.73	86.19	86.54

As can be seen in the table 4, the maximum accuracy in all cases is provided using $MT\text{-}ULTP_{8,1} + MT\text{-}ULTP_{16,2}$ based on three different binarization thresholds. Also, in all cases, multi threshold descriptors (MT-ULTP) provide better results in comparison with single threshold descriptor (ULTP). The results in the third part of the table 4, shows that MT-ULTP provides better accuracy than ULTP, even in the combined manner. The experimental results in Table 4, prove the our claimed observation #2, that using multi thresholds increase the classification accuracy because of using texture information in different level of power and magnitude.

5.3. Comparison with state-of-the-art methods

To performance of the proposed approach is compared with state-of-the-art methods in cell phenotype classification. In order to provide fair comparison, the same validation conditions (K-folds) and dataset (2d-Hela) are considered in this experiment. The experimental results using MLBP is reported based on our implantation in a same conditions. The reported results on 2D-Hela in [23] is not achieved based on 10-folds. So, to have a fare comparison, CapsNet [23] is implemented by author to evaluate classification accuracy in 10-folds. The comparison results demonstrate that the proposed approach provides higher classification accuracy than most of the methods in this area. In most cases, subject to the condition of validation, the reported result is presented in the table below.

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Table 5. Comparison results (%) of different cell phenotype classification methods on 2d-hela dataset

Approach	Classification Accuracy
SLF + BPNN [2]	86.11
LBP^{riu} [3]	82.7
OLPP(dim=15) [3]	72.8
OLPP(dim=30) [3]	82.15
Random Subspace of LMC [1]	**90.24**
SIFT(BoW(VQ)+SPM+SVM) [17]	83.79
LBP(BoW(VQ)+SPM+SVM) [18]	81.47
SAHLBP(BoW(VQ)+SPM+SVM) [16]	84.49
SIFT+SAHLBP(BoW(VQ)+SPM+SVM) [16]	86.20
SIFT(BoW(LLC)+SPM+Softmax) [7]	87.63
CapsNet [23]	86.21
$MLBP_{8,1}$	79.93
$MLBP_{8,1}$ + $MLBP_{16,2}$	84.33
MT-$ULTP_{8,1}$ + MT-$ULTP_{16,2}$ (proposed approach)	86.77

As can be seen in Table 5, random subspace of LMC [1] provides better classification accuracy in comparison with the proposed MT-ULTP. Runtime and computational complexity are two factors that play important role in cell phenotype classification. LMC method use fusion of some existing texture descriptors to provide a discriminative subset of features [1]. Also, ensemble machine learning methods is used for classification phase. So, the computational complexity of the LMC [1] is very high. In this respect, two metrics are evaluated here:

- First, based on reported results in [1], the number of dimensions in extracted feature vector using LMC is 242. Where, the number of dimensions in extracted feature vector using MT-$ULTP_{8,1}$ + MT-$ULTP_{16,2}$ with 3 binary thresholds are 156 dimensions. It is just 52 dimensions using MT-$ULTP_{8,1}$ + MT-$ULTP_{16,2}$ with single threshold.
- Secondly, 100 random images are selected form 2D-hela dataset. Next, LMC method is applied to extract features. Also, it is done using MT_ULTP too. Results show that average runtime of applying LMC is 873 milliseconds, where MT-ULTP is done it in 548 milliseconds.

As can be seen in Table 5, the LLC encoded BoW features in combination of Softmax regression [7] provides better accuracy about 0.86 percent in comparison with the proposed MT-ULTP. The proposed approach in [7] has 4 steps. First, SIFT features are extracted from image. Next, a bag of visual words are generated. Then, an innovative encoding algorithm is used. Finally, Softmax regression is employed to classify input cell image. As can be seen the runtime of the [7] is very higher than our proposed approach, because of using different sub-steps. To prove this claim, 100 random images are selected form 2D-hela dataset. Next, SIFT (BoW(LLC)+SPM+Softmax) method [7] is applied to extract features. Also, it is done using MT_ULTP too. Results show that average runtime of applying SIFT(BoW(LLC)+SPM+Softmax) is 983 milliseconds, where MT-ULTP is done it in 548 milliseconds.

5.4. Performance Comparison of the proposed approach against human experts

Classification of cells phenotype in fluorescence by human experts has four drawbacks as follows:

- Financial costs for the use of human experts
- The time cost of diagnosis by an expert is high.
- Expert human is not always available.
- The quality of an expert's diagnosis is not always constant. For example, if the expert is tired, the accuracy of the diagnosis decreases.

The proposed approach is a full automatic approach for cell phenotype classification, which decrease financial cost and time consuming. Also, it is always available to use everywhere with constant and stable diagnosis power. An innovative experiment is defined here. First, 100 random cell images are selected from 2D-Hela dataset. Then all samples were classified by two human experts. The samples were also classified using our proposed approach too. The average accuracy of the classification of human experts was 87.99 percent that provided in 430 seconds. The proposed method also classified these samples with 87 percent accuracy in exactly 180 seconds (617 milliseconds per image). This shows that the proposed method can detect cell phenotype types in a same range with human expert accuracy, and in a much shorter time, that make it usable in real laboratories.

6. Conclusion

The main aim of this paper is to propose a new approach for cell phenotype image classification. In this respect, a new image texture descriptor is proposed titled multi threshold uniform local ternary patterns (MT-ULTP). MT-ULTP is a texture descriptor with the aim of considering fluorescence microscope imaging and cell phenotype properties. MT-ULTP is a skillful combination of LTP and MLBP with novelty in feature extracting and pattern selection. MT-ULTP, extracts upper and lower uniform local binary patterns. Moreover, locality differences are captured based on multi different binarization thresholds. The performance of the proposed approach is evaluated on 2d-Hela dataset. Results show four following advantages:

- The proposed approach provides higher classification accuracy than many well known methods in cell phenotype classification.
- The proposed approach keeps benefits of LTP descriptors such as rotation invariant, low noise sensitivity and gray-scale invariant.
- Ignoring non-uniform patterns in the feature extraction process of LTP and some other lbp-like descriptors increases the classification accuracy of the cell phenotype classification.
- The combination of features derived from applying different binarization thresholds in local pattern extraction process of LTP, provides better results in comparison with using a unique threshold.
- Using multi thresholds to extract different levels of texture information and omitting non-uniform patterns are two main properties of the proposed MT-ULTP. So, the proposed MT-ULTP descriptor is a general texture descriptor, which can be used in many other computer vision applications with similar conditions to the cell phenotype classification problem. For example, medical image retrieval and visual surface defect detection are two problems where texture information in different levels should be extract.

In future works, our idea can be extended and applied for other multimedia applications, such as data exchange [19], image segmentation [20], image detection [21], and image dehaze[22].

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