

Fine grading of colorectal biopsy images using colour texture analysis

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Abstract. Severity of dysplasia is an important factor in the diagnosis of colorectal tumours, but visual examination of dysplasia is a time consuming, subjective process that is prone to inter-observer variation. We present our findings after an investigation into the ability of multiresolution colour texture features to classify images of colorectal tissue into a much finer classification than considered in previous studies. Here we consider five levels of dysplastic severity, namely: normal, mild, moderate, severe and cancer. Using a multiresolution colour texture based approach developed in our previous research, test images previously labelled by a trained clinician are classified into these five classes with an accuracy of 75%.

1 Introduction

Worldwide, colorectal cancer is the third most common malignant neoplasm. In the UK, colon cancer is the second most common cancer related cause of death, and kills around 17,000 people annually, with approximately 34,000 new cases each year. After diagnosis, around 60% of patients die within 5 years [1]. As with most other types of cancer, early diagnosis of colon cancer can drastically increase the chances of successful treatment [1].

This paper presents the results of an investigation into the discriminating ability of multiresolution colour texture features in the fine grading of dysplasia as displayed in colorectal biopsy images.

Previously, we have shown colour [2] and multiresolution [3] texture features to be closely correlated with dysplastic severity. This study examines the application of these features to five classes of severity - a much finer classification than considered in previous studies.

Related studies have attempted to classify such images using morphometric analysis [4] or texture analysis limited to grey-level, single resolution techniques [5] [6]. These investigations have considered only two classes, corresponding to normal and abnormal tissue. Multispectral texture analysis has been investigated in the domain of prostate cancer [7]. Again, this work deals with only a single spatial resolution, although the analysis involves three classes of image.

2 Method

We have shown in previous work [2] [3] that colour texture analysis can be used to classify images into three classes of dysplastic severity with very high levels of accuracy. To achieve the more complex task of assigning cases into more, smaller classes than previously used, it has been necessary to use more complex image analysis techniques. Related work in this area [6] successfully applied grey-level texture analysis to colon images, but our investigation showed that it was not sufficient when using more than two classes [2]. A technique commonly employed by pathologists to increase the visual contrast between areas of differing cytological content in colon biopsies is dual staining with Haematoxylin and Eosin. This dual staining procedure highlights cell nuclei blue and cytoplasm pink or red. The information that could be extracted from the pattern of hue and saturation is lost when colour information is discarded, as it has been in previous research. By using colour texture analysis, we have been able to improve the accuracy of classification [2].

Our previous research has also shown that using multiresolution texture analysis also increases classification accuracy [3]. Dysplasia is exhibited at both histological and cytological levels, and pathologists analyse both of these aspects by using multiple objectives. Multiresolution texture analysis exploits this behaviour.

2.1 Image Acquisition

In total, 60 $5\mu\text{m}$ slices from colorectal biopsy tissue were investigated. These samples exhibit various stages of dysplastic progression. Staining was performed using Haematoxylin and Eosin. The slides were digitised and classified by a qualified histopathologist with a specialism in gastro-intestinal cancers. The resulting images are 768×576 pixels, examples of which are shown in Figure 1. In our previous experiments [2] [3], regions of the slide were selected to ensure that the image contained only tissue of one class. In this study we consider the more challenging situation in which entire samples are used.

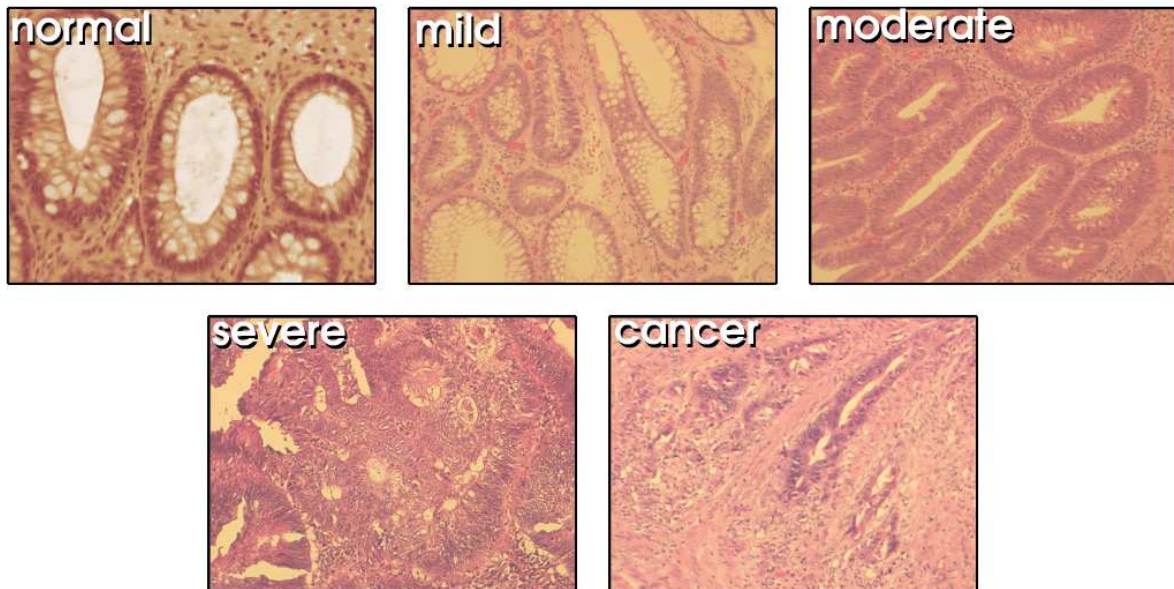


Figure 1. An example image from each class.

2.2 Texture analysis and classification

Entropy	$\sum_i \sum_j P(i, j) \log P(i, j)$	Contrast	$\sum_i \sum_j (i - j)^2 P(i, j)$
Correlation	$\sum_i \sum_j \frac{(i - u_x)(j - u_y)P(i, j)}{\sigma_x \sigma_y}$	Homogeneity	$\sum_i \sum_j \frac{P(i, j)}{1 + i - j }$
Dissimilarity	$\sum_i \sum_j P(i, j) i - j $	Angular Second Moment	$\sum_i \sum_j P(i, j)^2$
Energy	\sqrt{ASM}	Horizontal mean (μ_x)	$\sum_i \sum_j i P(i, j)$
Vertical stdv (σ_y)	$\sqrt{\sigma_y^2}$	Horizontal variance (σ_x^2)	$\sum_i \sum_j P(i, j) (i - \mu_x)^2$
Vertical variance (σ_x^2)	$\sum_i \sum_j P(i, j) (j - \mu_y)^2$	Horizontal stdv (σ_x)	$\sqrt{\sigma_x^2}$
Vertical mean (μ_y)	$\sum_i \sum_j j P(i, j)$		

Table 1. Texture measurements extracted from co-occurrence matrices

Co-occurrence matrices [8] [9] have been used in the past to extract texture information for many applications, including medical image analysis [10] [11]. The co-occurrence matrix is constructed by first determining a pairing relationship. The pairing relationship, often expressed as a distance, d , and angle, θ , is used to pick pairs of pixels from the image. All pixel pairs matching the pairing relationship are analysed, and their values used to populate a matrix such that the values of the two pixels (source and target) are used as row and column identifiers in the matrix. The cell identified by the values of the pixel pairs is incremented for each valid pair. The co-occurrence matrix then contains the number of times two pixels with any given value occur in the image, separated by the pairing relationship.

For our work rotational invariance is necessary, and so co-occurrence matrices are calculated with the angle between pixel pairs set to $\theta, \theta + 90, \theta + 180$ and $\theta + 270$ degrees. The final co-occurrence matrix is calculated by averaging these four intermediate matrices.

Normalisation of a matrix is carried out by dividing each element by the total number of valid pairs. So, for a normalised matrix, P , $P(i, j)$ is the probability of the source pixel having value i and the target pixel having value j for any given pair of pixels matching the pairing relationship. A normalised co-occurrence matrix is constructed for each image in our data set. From this matrix each of the features in Table 1 is extracted.

In an earlier study [2], we demonstrated that colour texture information improves the accuracy of classification. Building on this approach, we extract the features described in Table 1 from each channel of the RGB and HSB representations of the data.

Features that indicate dysplasia are visible at different levels of magnification, corresponding to cytological and histological disorganisation. Pathologists, therefore, use multiple objectives to assess dysplasia at these levels. The size, shape and stain uptake of the *cells* change as dysplasia becomes more severe, which affects the visible texture of the images at a high resolution. By pathologists, this is evaluated at high magnification. Using texture analysis, this is measured with values of d between 1 and 4. The abnormal growth and rate of replication also cause the *tissue* to appear disorganised at a lower magnification, in the merging and branching of crypts, and in more severe cases, loss of differentiation. This structural exhibition of dysplasia has been measured using d at 40, 60, 80 and 100, with neighbouring pixels also taken into account using a Gaussian average at the source and target with a radius, $r = 15$ and $\sigma = 15$.

Classification has been carried out using discriminant analysis to determine which features correlate with dysplastic severity, and to assess the ability of these features to classify the images.

3 Results

Specificity and sensitivity are difficult to define where the classification involves more than two groups. Instead we present figures that indicate similar characteristics, but which are easily calculated and understood. If we define downward misclassifications as cases of abnormal tissue being classified as normal, in a two class system for example, and upwards misclassifications as the opposite, we can see that fewer downwards misclassifications is similar to increased sensitivity, and fewer upwards misclassifications is similar to increased specificity. In this experiment, downwards classifications accounted for 10% of cases, and upwards classifications accounted for 15%.

Table 2 shows the actual and predicted classifications. Overall, this is a classification accuracy of 75%.

Actual ↓ Predicted →	Normal	Mild	Moderate	Severe	Cancer
Normal	12	0	0	0	1
Mild	1	10	0	4	0
Moderate	0	2	13	1	0
Severe	1	2	3	4	0
Cancer	0	0	0	0	6

Table 2. Actual classifications and those predicted by discriminant analysis

Discriminant analysis reduced the necessary features to just nine, shown in Table 3

Correlation of the green component at 100 pixels	Entropy of the hue component at 4 pixels
ASM of the green component at 100 pixels	ASM of the green component at 40 pixels
Contrast of the red component at 1 pixel	Entropy of the blue component at 80 pixels
Mean saturation at 100 pixels	Energy of the green component at 4 pixels
ASM of the green component at 4 pixels	

Table 3. Discriminating features

4 Discussion

The results presented above clearly show that there is a strong correlation between multiresolution colour texture features and the severity of dysplasia in colon biopsy images. While this is a drop in accuracy from our previous results which achieved an accuracy of over 98%, it is important to note that the complexity of the task has been

increased by removing the selection of a region of interest and by increasing the number of groups from three to five. Hence, a direct comparison is inappropriate.

With reference to Table 3, it is interesting to note that although previous research has used grey-level features to classify images of this type, none of the features accounting for the majority of variability in this study are taken from the brightness channel.

Five of the nine features selected by discriminant analysis use large values for d , indicating that the measurements of lower resolution, structural deformities are at least as important as the more commonly used fine texture measurements. Again, these features have previously been overlooked.

Bosman [12] states that problems with inter- and intra-observer variation in the assessment of dysplasia are mainly due to two things: a lack of clearly defined morphological criteria, and the enforcement of a discrete classification on a process that is intrinsically continuous. We have attempted to overcome the first of these problems by using textural features rather than morphological features, thereby removing the need to obtain an accurate segmentation of structures in the images. We propose that a possible solution to the second problem may be found through an investigation of the relative weightings associated with the discriminating features identified in this study.

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