An Improvement on the Detection of Skin Cancer Based on Raman Spectroscopy

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Abstract: - In this study, we present a BCC detector based on confocal Raman spectroscopy using maximum *a posteriori* probability (MAP) and fuzzy algorithm. The preprocessing step consists of data normalization with *minmax* method and dimension reduction with principal components analysis (PCA). To enhance the classification performance, we divide Raman spectra into two significant protein bands, i.e., Amid I and Amid III mode and extract features independently. In this way, classification experiments with fuzzy and MAP algorithms were carried out using 216 confocal Raman spectra. According to the experimental, the proposed two band approach enhance the classification performance of the fuzzy and MAP algorithm meaningfully.

Key-Words: - **BCC, Raman Spectroscopy, Fuzzy Algorithm, Pattern Recognition**

1 Introduction

Raman spectroscopy is a vibrational spectroscopy. It is widely used in chemical and material science. Recently Raman spectroscopy has been applied in the area of biomedical research. Especially Raman spectroscopy is actively studied for in-vivo diagnosis of cancers.

Basal cell carcinoma (BCC) is one of the most common skin cancers. Some basic research on diagnosis of BCC based on Raman spectroscopy has been performed [1-4]. Those papers said that Raman spectroscopy is an effective tool for skin cancer detection. Among various kinds of Raman spectroscopy, confocal Raman spectroscopy is the most promising technique since it does not suffer from background noise problem. According to [2], confocal Raman spectra provide promising results for the detection of precancerous and noncancerous lesions without special treatment.

Various kinds of classification algorithms were implemented and compared in [3] but fuzzy type algorithm were excluded. So we investigate the performance of an automatic classifier based on fuzzy algorithm in this paper. Then we compared with the classification error rates of the proposed method with Maximum *a posteriori* Probability (MAP) method. In addition to it, we divide Raman spectra into two significant protein bands to enhance the classification performance. The protein bands correspond to Amid I and Amid III mode. Experimental results involving 216 confocal Raman spectra showed that the proposed two band approach yield better classification performance than one band approach.

2 Preprocessing of Data

The preparation of data for the classification includes confocal Raman measurement and preprocessing. Raman spectra were obtained using a commercial Renishow 2000 Raman microscope system. After Raman measurements, normalization and windowing was carried out for the spectra. Then dimension reduction was followed using principal component analysis (PCA) for feature extraction. In the following, we will describe the procedures in detail.

The tissue samples were prepared with the conventional treatment, which is exactly the same as [2]. BCC tissues were sampled from 10 patients using a routine biopsy. Cross sections of 20 μm were cut with a microtome at -20 ℃ and stored in liquid nitrogen. Two thin sections of every patient were used for experiments. One section was used for classification and the other section was stained with H&E and used as a Raman reference after locating the boundaries between BCC and normal (NOR) by an expert pathologist with a routine cancer diagnosis.

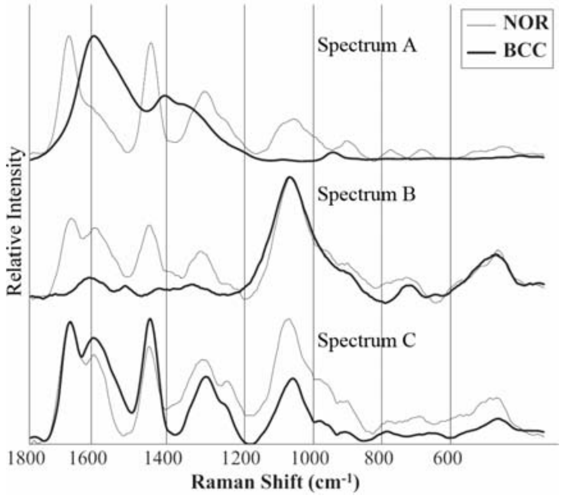

Fig. 1. Confocal Raman spectra from three patients at different spots.

The confocal Raman spectra for the skin samples are shown in Fig. 1 where no strong background noise is observed. In the Fig. 1A, there is a clear distinction between BCC and NOR tissues. Most of the spectra belong to this case. The Fig. 1B shows the case when a BCC spectrum is measured in the vicinity of the boundary of BCC and NOR.

Since a peak near 1600 cm^{-1} is a distinctive feature of BCC spectra as shown in the Fig. 1A, the BCC spectrum in Fig. 1B could be classified as BCC though the feature is not so evident. The Fig. 1C shows an outlier, where the BCC spectrum is obtained in the middle of the BCC region but looks very similar to that of NOR. It is probably caused by the fact that the spectrum was obtained from the vicinity of the boundary between BCC and NOR.

A skin biopsy was performed in the perpendicular direction from the skin surface, and it is the same for the spectral measurements. Raman spectra of BCC tissues were measured at different spots with an interval of 30~40 μm. In this way, 216 Raman spectra were collected from 10 patients.

After the measurements, Raman spectra were clipped at Raman shifts from 1750-1200 cm^{-1}, which region is known to contain all important protein bands, e.g., amide III, lipid and protein, amide I, phospholipid and nucleic acid mode. Then the spectra were normalized with *minmax* method so that it falls in the interval [-1, 1].

In addition to the above one band approach, we divide Raman spectra into two significant protein bands corresponding to the regions, i.e., 1750-1500 cm^{-1} and 1400-1200 cm^{-1}. The protein bands correspond to Amid I and Amid III mode [2]. Since those bands have some physical importance, we expect that two band approaches would yield better classification performance than one band approach.

For feature reduction, we applied PCA. Since PCA identifies orthogonal bases on which projections are uncorrelated, it is the most preferred feature reduction method. Principal components can be obtained via eigenvalue decomposition of the following scatter matrix **S**.

$$\mathbf{S} = \sum_k (\mathbf{d}_k - \boldsymbol{\mu})(\mathbf{d}_k - \boldsymbol{\mu})^T, \tag{2}$$

where $\mathbf{d}_k$ is an input pattern and $\boldsymbol{\mu}$ is the mean of $\mathbf{d}_k$.

If we let **D** be a diagonal matrix of eigenvalues in descending order and **E** be an orthogonal matrix whose columns are the eigenvectors corresponding to eigenvalues, we can obtain principal components $\mathbf{x}_k$ as follows.

$$\mathbf{S} = \mathbf{E}\mathbf{D}\mathbf{E}^T, \tag{3}$$

$$\mathbf{x}_k = \mathbf{E}^T\mathbf{d}_k. \tag{4}$$

Finally, feature reduction can be accomplished by discarding the unimportant elements of $\mathbf{d}_k$. The number of retained principal components could be determined experimentally according to classification method.

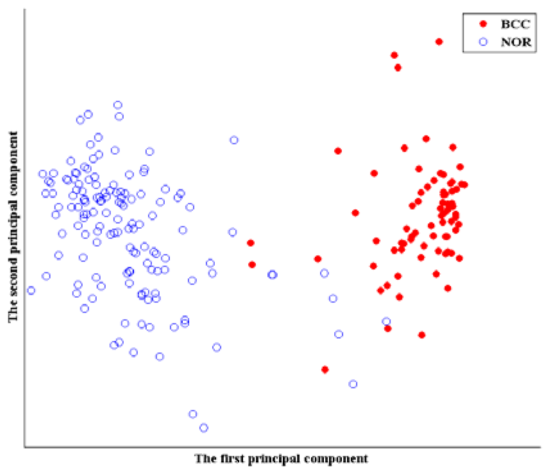

Fig. 2. The distribution of the first two components of PCA transformed spectra.

3 Classification Methods and Experimental Results

To see how well the feature vectors of two different classes, BCC and NOR, are separated, we plotted them in the Fig. 2, where x, y correspond to the first and the second component of the transformed feature vector. The figure clearly shows that the input feature vectors are well separated even though some BCC and NOR spectra regions are overlapped.

Two types of classifiers including MAP and fuzzy were examined in this work. In the MAP classification, we select the class, ω_i, that maximizes the posterior probability $P(\omega_i \mid \mathbf{x})$ [5]. Given the same prior probability, it is equivalent to the selection of the class that maximizes the class conditional probability density. Let ω_1, ω_2 be BCC class and NOR class respectively. MAP classification rule is expressed as follows.

$$\text{Deside} \begin{cases} \omega_1, & \text{if } P(\mathbf{x} \mid \omega_1) \geq P(\mathbf{x} \mid \omega_2), \\ \omega_2, & \text{otherwise.} \end{cases} \tag{5}$$

Since input vectors are well separated and distributed around their class mean as in Fig. 2, we could model the class conditional probability with multivariate Gaussian probability density function. The parameters, mean vector $\boldsymbol{\mu}$ and covariance matrix $\boldsymbol{\Sigma}$, were estimated in the maximum likelihood sense. Let n_i be the number of data in ω_i. Then the decision rule is expressed with the discriminant function, $g_i(\mathbf{x})$, as follows.

Decide $\boldsymbol{\omega}_1$ if $g_1(\mathbf{x}) \geq g_2(\mathbf{x})$, where

$$g_i(\mathbf{x}) = -\frac{1}{2}\mathbf{x}^T \boldsymbol{\Sigma}_i^{-1}\mathbf{x} + \boldsymbol{\Sigma}_i^{-1}\boldsymbol{\mu}_i \mathbf{x} + r_i, \tag{6}$$

$$r_i = -\frac{1}{2}\boldsymbol{\mu}_i^T \boldsymbol{\Sigma}_i^{-1}\boldsymbol{\mu}_i - \frac{1}{2}\ln\left|\boldsymbol{\Sigma}_i^{-1}\right|, \tag{7}$$

$$\boldsymbol{\mu}_i = \frac{1}{n_i}\sum_{\mathbf{x}\in\omega_i}\mathbf{x}, \tag{8}$$

$$\boldsymbol{\Sigma}_i = \frac{1}{n_i}\sum_{\mathbf{x}\in\omega_i}(\mathbf{x}-\boldsymbol{\mu}_i)(\mathbf{x}-\boldsymbol{\mu}_i)^T. \tag{9}$$

In the fuzzy classification, a bell-shaped function is used as an input membership function. Well known Sugeno-type fuzzy inference system (FIS) was employed to ease the training process. The membership functions and associated parameters were adjusted adaptively via a combination of the least-squares method and the back-propagation gradient descent method, which is known as neuro-adaptive learning technique. Overall structure used in this work is shown in Fig. 3.

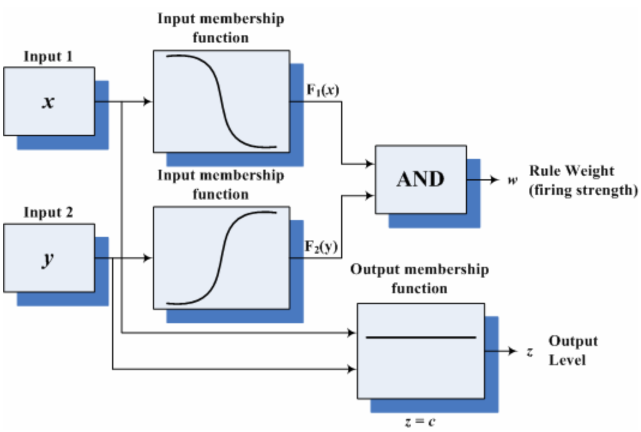

Fig. 3. The structure diagram of the Sugeno-type fuzzy inference system.

The FIS were trained to output +1 for BCC class and +2 for NOR class. If we let the final output value of the FIS to be d, the decision rule is given as follows.

$$d = \frac{\sum_i w_i z_i}{\sum_i w_i}. \tag{10}$$

$$\text{Decide} \begin{cases} \omega_1, & \text{if } d < 1.5, \\ \omega_2, & \text{if } d > 1.5, \end{cases} \tag{11}$$

where ω_1 is the BCC class and ω_2 is the NOR class.

A total of 216 data were divided into two groups. One group was designated as a training set and the other group was considered as a test set. The data from 9 patients out of 10 patients were used as a training set and the data from the remaining patient were used as a test set. To avoid model overfitting in FIS, training data were further divided into two groups. The first data group was used for training FIS and the second data group was used for validation.

Once the classification was completed, the data from one patient were eliminated from the training set and used as new test data. The previous test data were then inserted into the training set. In this way, the data from every patient were used as a test set. That is the process of 'leaving one out' method. The average number of BCC and NOR spectra in the test set was 8 and 14 and that in the training set was 68 and 126 respectively.

Table 1. The classification results of MAP and fuzzy algorithm.

	1 band approach	2 band approach
MAP	96.3%	96.8%
fuzzy	96.3%	97.2%

To show the effectiveness of the two band approach, experiments with one band approach were also carried out and the results were compared. The classification results are summarized in the Table 1. The number of principal components was set to 2 for one band approach. In the case, MAP and fuzzy algorithm yielded the same classification rates of 96.3%. In the case of two band approach, the number of principal component was set to 1 for each band. Since there are two bands, overall number of principal components is the same as in one band approach. According to the above results, the true classification rate of MAP was increased from 96.3% to 96.8% and that of fuzzy was from 96.3% to 97.2%. These results indicate that two band approaches is more promising than one band approach.

4 Conclusion

In this paper, we have investigated fuzzy and MAP classification method with confocal Raman spectra to detect BCC which is one of the most common skin cancers. For classification performance enhancement, we divided Raman spectra into two significant protein bands which correspond to Amid I and Amid III mode. Experimental results involving 216 confocal Raman spectra showed that the proposed two band approach yield better classification results than one band approach. We are currently investigating more objectively meaningful region search technique to further improve the performance of the classifiers.

Acknowledgment

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