A Border Irregularity Measure Using a Modified Conditional Entropy Method as a Malignant Melanoma Predictor

Benjamin S. Aribisala* and Ela Claridge **

School of Computer Sciences,
The University or Birmingham,
Birmingham B15 2TT, U.K.

Abstract. In the diagnosis of malignant melanoma, a skin cancer, the degree of irregularity along the skin lesion border is an important diagnostic factor. This paper presents a new measure of border irregularity based on conditional entropy. The measure was tested on 98 skin lesions of which 16 were malignant melanoma. The ROC analysis showed that the measure is 70% sensitive and 84% specific in discriminating the malignant and benign lesions. These results compare favourably with other measures and indicate that conditional entropy captures some distinguishing features in the boundary of malignant lesions.

1 Introduction

Melanoma is a malignant tumour of melanocytes. The tumour initially starts from the epidermis and if not detected and removed early it invades the dermis. The patient's survival rate is inversely proportional to the depth of the tumour. Early detection of melanoma is the most important factor affecting the survival of a patient.

Malignant melanoma can be characterised by shape, edge, colour and surface texture of the lesion. The border irregularity of pigmented skin lesions is one of the most significant diagnostic factors in clinical diagnosis of melanoma [6, 7].

It has been empirically discovered that clinicians have difficulties in visually assessing border irregularity of skin lesion outlines and that their assessments are not invariant to reflection and rotation [7, 4]. Much research on quantitative measures of irregularity has been carried out to overcome these shortcomings [7]. The most common approaches include the Compactness Index (e.g. [13]), Fractal Dimension and Structural Fractal Dimension (e.g.[4]), measures based on radial distance (e.g. [12]), Sigma Ratio and Indentation Irregularity Index (III) [11]. III is the most successful algorithm to date for classifying skin lesions on the basis of their border irregularity.

* Email: B.S.Aribisala@cs.bham.ac.uk
** Email: E.Claridge@cs.bham.ac.uk

The term "*Irregularity*" is contextual and can express different meanings. If irregularity is to be quantified, it is necessary first to develop its formal definition, or at least provide its formal description. Five attributes of irregularity have been proposed [8]. One of these attributes which is of interest here is unpredictability. The elements of a sequence corresponding to a regular shape or pattern are predictable, whereas in an irregular shape or sequence they cannot be easily predicted. That is, the extent to which a sequence can be predicted may suggest its degree of irregularity.

This paper presents a new measure of border irregularity based on conditional entropy. In contrast to the existing measures, the proposed measure is based on a formal criterion of irregularity outlined above. A prior knowledge of some points along the border of a normal skin lesion can be used to predict more points along the same border with high degree of certainty, whereas predictions for abnormal skin lesions will have reduced certainty leading to high value of entropy. That is conditional entropy increases with the degree of unpredictability.

Section 2 presents a brief description of the entropy while section 3 presents the proposed method of computing conditional entropy. Section 4 describes the experimental data while section 5 describes the experiments. Results and discussion are presented in section 6. Finally, section 7 presents the conclusion.

2 Entropy

Entropy can be described as a measure of information, the degree of uncertainty or unpredictability of a system or sequence. Entropy is directly proportional to unpredictability. That is, a sequence which is highly unpredictable (or random) has higher entropy than an easily predictable sequence. The original entropy (equation (1)) called the Shannon's entropy was designed by Claude Shannon in 1948 [2]. The wide range of applications of entropy has motivated different modifications to Shannon's entropy. Some of its modifications are Renyi's entropy [3], mutual information, conditional entropy and joint entropy [5]. Here we are interested in conditional entropy but first provide some background related to joint entropy.

$$H(x) = -\sum_{x \in X} P_r(x) log_2 P_r(x) \tag{1}$$

Let X and Y be random variables such that $x \in X$ and $y \in Y$ and let $P_r(x)$ be the probability of a particular value x. The joint entropy H(X, Y) (equation (2)) of X and Y measures the unpredictability associated with the joint probability $P_r(x, y)$ of X and Y while the conditional entropy of Y given X denoted H(Y/X) (equation(3)) measures the unpredictability associated with the conditional probability $P_r(y/x)$ of Y given X. Since H(X)$\geq$ 0, equation (4) implies that conditioning reduces entropy.

$$H(X, Y) = -\sum_{x \in X} \sum_{y \in Y} P_r(x, y) log_2 P_r(x, y) \tag{2}$$

$$H(Y/X) = -\sum_{x \in X} \sum_{y \in Y} P_r(x,y) log_2 P_r(y/x) \quad (3)$$

$$H(X,Y) = H(X) + H(Y/X) \quad (4)$$

Entropy has two major problems. First, it is not sensitive to the relative position of elements in a sequence, e.g. a periodic sequence 10101010101010101010 and a random sequence 11010011011001011 have the same entropy. This is due to the fact that entropy is computed by counting the number of elements of the sequence that belong to each distinct category of a sequence determined by the value of the bin size r. This constitutes a weakness of any entropy based measure (such as conditional entropy and joint entropy), most especially in pattern recognition and classification problems where the relative position of elements of a signal is important. Secondly, the value of entropy is strictly dependent on the bin size. A wrong choice may lead to a wrong and misleading result. We investigated these problems and proposed a new technique of computing conditional entropy. This was implemented on both simulated and real data. Simulated data was used to investigate the relationship between the proposed conditional entropy and the amount of noise level in a signal while the real data was used for characterisation of malignancy in pigmented skin lesions.

3 Computing Conditional Entropy

Conditional entropy can be computed using equation (3). This implies that two sequences are needed for its computation, X and Y. We describe equation (3) as a *sequence based conditional entropy* (SBCE) because H(Y/X) is computed by computing the entropy of sequence Y based on the knowledge of sequence X (note that we can have more than two random variables in which case the conditional entropy of one variable can depend on two or more variables). The sequence based entropy is not a good measure of irregularity because it is independent on the relative positions of the elements of a sequence (see section 2). Here we propose a new type of conditional entropy which depends on the relative positions of elements of a sequence, we call it "*element based conditional entropy*" (EBCE).

Let X = $x_1, x_2, ..., x_n$ be a random sequence of length n. We define the *element based conditional entropy* of a sequence X, denoted $H_e(X)$, as the overall conditional entropy of successive elements of X based on the preceding elements (equation (5)). The EBCE is similar to the SBCE but they have two major differences. The first difference is that unlike the SBCE, the EBCE is sensitive to the relative positions of elements of X. Secondly the EBCE can be computed for just one sequence while the sequence based conditional entropy is designed for at least two sequences.

$$H_e(X) = -\sum_{t=m}^{t=n} P_r(x_t, (x_{t-1}, ..., x_{t-m+1})) log P_r(x_t/(x_{t-1}, x_{t-2}, ..., x_{t-m+1})) \quad (5)$$

where n is the length of X and m is the length of different subsequences of X. The case for m=2 is represented in equation (6).

$$H_e(X) = -\sum_{t=2}^{t=n} P_r(x_t, x_{t-1}) log P_r(x_t/x_{t-1}) \tag{6}$$

Like other entropy based measures H_e is directly proportional to unpredictability and H_e of a regular sequence is 0. Like other entropy based measures, H_e is also strictly dependent on the bin size r.

The computation of EBCE using equation (5) requires a good choice of m, the bin size r and a good definition of the conditionality variable

$$q_t = (x_t/(x_{t-1}, x_{t-2}, ..., x_{t-m+1})) \tag{7}$$

We have investigated different ways of defining q_t using different choices of m and r. Here we present the definition that gave us the best result. We use $H_e^r(m_0 \rightarrow m_f)$ to denote EBCE for fixed r and variable m where m_0 and m_f are the minimum and maximum m such that $2 \leq m \leq n$, n is the sequence length. $\coprod_{i=1}^{i=n-m+1} \{x_i x_{i+1} x_{i+2} ... x_{i+m-1}\}$ will be used to denote a set of all subsequences of X.

Let S be a set of all subsequences of X each of length m (see equation(9)). $H_e^r(m_0 \rightarrow m_f)$ can be computed by defining q_t as the difference between the last and the first element of each subsequence (see equation (8))

$$q_t = (x_t/(x_{t-1}, x_{t-2}, ..., x_{t-m+1})) = (x_t - x_{t-m+1}) \tag{8}$$

$$S = \coprod_{i=1}^{i=n-m+1} \{x_i x_{i+1} x_{i+2} ... x_{i+m-1}\} \tag{9}$$

For example if $X = \{x_1, x_2, x_3, x_4, x_5\}$ and q_t is computed for m=3, using equation (9) $S = \{x_1x_2x_3, x_2x_3x_4, x_3x_4x_5\}$ and $q_3 = \{x_3 - x_1, x_4 - x_2, x_5 - x_3\}$.

4 Data Description

Medical experts regard a skin lesion that is nearly circular or elliptical in overall shape as more likely to be normal than not [4]. In view of this we have taken the ellipse to be a shape model for a normal skin lesion and to represent the most regular instance of the lesion shape. Figure (1) shows examples of real lesion outlines, (a) regular and (b) irregular. Thus if we assume prior knowledge of a regular (normal) skin lesion, points along its border can be predicted with high certainty whereas prediction for irregular skin lesions will have relatively reduced certainty. That is irregularity increases with unpredictability, hence we frame irregularity as unpredictability.

The lesion border data is represented as a sequence of (1D) radial coordinates in a polar coordinate system centred at the centre of gravity of the lesion. The

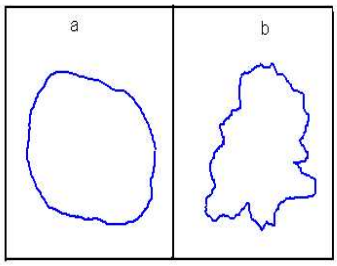

Fig. 1. Lesion Outline samples:(a) regular, (b) irregular

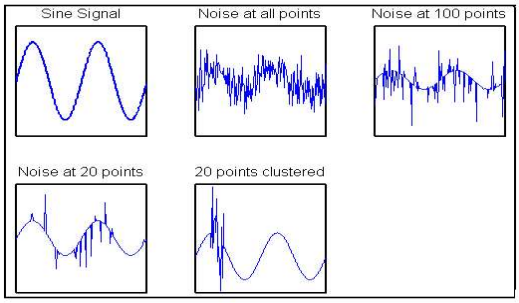

Fig. 2. Simulated data

coordinates constitute a sequence $O = O_1, O_2, ..., O_M$ where O_i, i=1, ..., M is an ith boundary point.

In a polar coordinate system the radial coordinates of an ellipse can be represented by a sine function. In view of this the simulated data is composed of sine signals each of length 200 with random noise added at different points. The data was grouped into 5 categories with each category having 50 sequences. The first category is a set of 50 sine signals. These 50 signals were used to generate the remaining four categories by adding Gaussian random noise (with standard deviation ranging from 1 to 10) at all points, at 100 randomly selected points, at 20 randomly selected points, and at 20 randomly selected points but clustered together (See Figure (2) for some examples of these signals). The sine signals without noise represent "*normal*" skin lesions while those with noise represent irregular skin lesions with the amount of noise suggestive of the degree of irregularity. The conditional entropy for all the simulated and the real data was computed using the proposed method. Our hypothesis is that conditional entropy increases with the degree of irregularity.

5 Experiments

Simulated data consisted of 250 sine signals with different amount of noise. The real data represented 98 skin lesion of which 16 were histologically confirmed cases of melanoma [9]. The radial coordinates corresponding to lesion boundary were extracted using a boundary modelling technique [1]. The data was normalised by subtracting the mean and dividing by standard deviation to make it scale invariant. Using equations(8, 9 and 5), EBCE was computed for both the simulated and the real data. The value of r was set to r=0.01*SD (SD is the standard deviation of each sequence) and m = 2 to n was used. It was observed that in both cases $H_e^r(m_0 \rightarrow m_f)$ increased exponentially with increase in m (see Figures 3a and 3b). To determine the degree of irregularity $H_e^r(m_0 \rightarrow m_f)$ for each sequence was fitted using an exponential fit and the exponential parameter $H_e^\mu(i)$ was estimated. Additionally the standard deviation $H_e^\sigma(i)$ and the slope

$H_e^{slope}(i)$ (i is the lesion number) of each $H_e^r(m_0 \rightarrow m_f)$ with respect to r was computed.

To assess the discriminatory power of EBCE in characterisation of malignancy of pigmented skin lesion the ROC analysis was performed for all the three proposed estimators of irregularity: H_e^{μ}, H_e^{σ} and H_e^{slope}.

5.1 Experimental Survey

One interesting question, not answered through the above experiments, was whether any of the computed measures for real data corresponds to the human perception of the border irregularity in the skin lesions. To this end an experimental survey was carried out. 20 skin lesion outlines randomly selected from the full data set were given to 23 subjects, none of whom had medical training. The subjects were asked to rank the outlines based on their degree of irregularity. The level of agreement among the subjects was evaluated using rank correlation r_s based on Kendall coefficient of concordance W [10]. The value of r_s ranges from 0 (no agreement) to 1 (perfect agreement).

To test a "default" hypothesis, that irregularity simply depends on the magnitude of variations along the boundary, the standard deviation was computed for all the lesion outlines before normalisation.

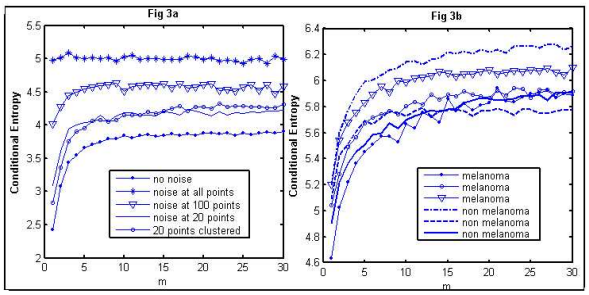

Fig. 3. Conditional Entropy

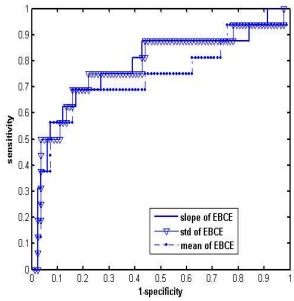

Fig. 4. ROC Curve

The Spearman coefficient of correlation was determined for each of the proposed irregularity estimators ($H_e^{\mu}, H_e^{\sigma}, H_e^{slope}$), the visual assessment (using the average ranking from the 23 subjects), and the standard deviation for the selected 20 lesions. Finally, the relationship between all estimators was examined using multiple linear regression analysis.

6 Results and Discussion

Figures (3a and 3b) show that EBCE increases exponentially as m increases in both the simulated and real data. This is a good result because intuitively

increase in m increases the elements of each subsequence hence the probability of each element decreases which leads to reduction in the degree of predictability. Additionally H_e^{μ} and H_e^{σ} increase with noise level in the simulated data while H_e^{slope} decreases with noise level. These suggest that all the three statistics are potentially useful estimators of noise levels of a signal. Since the noise level is an indicator of the level of unpredictability, it can hence be proposed that all the three statistics are potentially useful measures of degree of unpredictability of signals.

The ROC analysis of H_e^{μ} as a melanoma classifier showed 68% sensitivity and 84% specificity, H_e^{σ} gave 70% sensitivity and 82% specificity while H_e^{slope} gave 70% sensitivity and 84% specificity. Figure 4 shows the ROC plots for all the three statistics. These results show that EBCE can be used to measure the degree of unpredictability of a signal and that boundary sequences corresponding to abnormal lesions have high level of unpredictability (i.e. more irregular) when assessed using H_e^{slope}. Hence we propose the use of H_e^{slope} as a measure of irregularity.

In a way of illustration, the value of H_e^{slope} for the regular lesion in figure 1(a) is 0.03 and for the irregular lesion in figure 1(b) it is 0.01 on the scale where 0.06 corresponds to the most regular shape and 0.001 to the most irregular shape.

In the experiments examining the perception of irregularity, the coefficient of concordance W was 0.886, indicating good agreement between all 23 subjects. The assessment of irregularity by the subjects correlated moderately well with both the EBCE (H_e^{slope}) measure (Spearman correlation coefficient of 0.55) and standard deviation (0.466). Correlation was very good between the EBCE irregularity measure and standard deviation of the real data (0.87). The multiple linear regression analysis for all three tests showed good correspondence (0.51). These results suggest that humans have similar way of assessing shape irregularity, and that the human notion of irregularity is similar to the assessment by the indicators investigated here. The strong correlation between the EBCE measure and the standard deviation suggest that the conditional entropy based measure is good at measuring the variation along the lesion border.

We have compared the result of the proposed measure with one of the best published melanoma predictors based on irregularity, the Indentation Irregularity Index (III) [9]. The comparison used the area under the ROC curve, which is a global measure commonly used to assess the overall predictive power of classification schemes. The III computed for a superset of the set of lesions used in our experiments has the area under ROC curve of 0.73 [9], whereas the EBCE gave area of 0.76. This indicates that the conditional entropy based measure has a greater discriminatory power than the III index.

7 Conclusion

In this paper we have proposed a new measure of border irregularity based on conditional entropy. This measure has been devised to quantify lack of predictability. We have demonstrated that abnormality of skin lesion can be de-

scribed using irregularity along the skin lesion border. Given some prior knowledge of a normal skin lesion, points along its border can be predicted with high degree of certainty whereas prediction for abnormal skin lesion will have reduced certainty leading to high value of entropy. That is entropy increases with the degree of irregularity.

The ROC analysis of the conditional entropy based measure as a malignancy predictor gave 70% sensitivity and 84% specificity. This result shows that the conditional entropy based measure captures some distinguishing features in the boundary of malignant lesions and thus can contribute to lesion classification.

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