Classification of Cervical Cancer Cells Using HMLP Network with Confidence Percentage and Confidence Level Analysis.

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Abstract

In most previous studies, the analysis on the ability of neural networks to be used as a good cervical cancer diagnosis technique is only based on accuracy, sensitivity, specificity, false negative and false positive. In the current study, we go one step further by introducing analysis of diagnosis confidence percentage and diagnosis confidence level to analyse the ability of neural network to produce a good diagnosis performance. The current study used hybrid multilayered perceptron (HMLP) network to diagnose cervical cancer in the early stage by classifying cervical cells into normal, LSIL and HSIL cell. The proposed diagnosis confidence percentage and diagnosis confidence level analysis have been proved to give clearer picture on the strength or confidence level of each diagnosis, which is done by HMLP network.

Keywords

Cervical cancer, HMLP network, diagnosis confidence percentage, diagnosis confidence level, Pap test.

1. Introduction

Cervical cancer is the second common malignancy in women. However, in Malaysia, Ministry of Health reported cervical cancer is the first leading cancers in women (Ministry of Health, 1999). Malaysian government has launched the National Cancer Control Program to reduce...
the incidence and mortality of cancer including cervical cancer. The program aims to improve the quality of life of cancer patients. The program policies encompass prevention, early diagnosis, treatment, palliative care and rehabilitation. In order to reduce the incidence and mortality of cervical cancer, the program aims to increase the Pap test facilities and public education campaign.

In Malaysia, Papanicolaou test or better known as Pap test is commonly used as cervical cancer screening test. Several previous studies by Breen et al. (2001), Framer (2001), Kuie (1996) and Adami et al. (1994), showed that the chances for a woman of acquiring cervical cancer is reduced as she has Pap test regularly. However, studies by Othman et al., (1997, 1995), Kuie (1996) and Hislop et al. (1994) proved that sometimes the Pap test is not effective. The determination of abnormal cervical cells can sometimes be missed in certain situation. Three major reasons that decrease the accuracy of Pap test diagnosis result are bad Pap smear samples, technical errors and small size of CIN. Beside that, the screening procedure on the Pap smear sample requires an experienced pathologist and thus expensive and time-consuming.

Due to the problems, several previous studies have successfully developed automated and semi-automated screening systems in order to increase the diagnosis performance of Pap test. Three supplementary diagnosis systems for Pap test which are commonly used in medical field and currently approved by the Food and Drug Administration (FDA) are Papnet, AutoPap and ThinPrep (WebMD, 2002, HTAC, 2002). Beside those supplementary systems, several previous studies also proposed artificial intelligence as a cervical cancer diagnosis system. The most popular artificial intelligence systems that were used for that purpose are neural networks. Multilayered perceptron network (MLP) becomes the most popular neural networks to be used as cervical cancer diagnosis system (Li & Najarian, 2001, Mitra et al., 2000, Balasubramaniam et al. 1998). Papnet system also used MLP network trained using back propagation (BP) algorithm. In the current study, HMLP network trained using modified recursive prediction error (MRPE) algorithm is proposed to diagnose cervical cancer.

In almost all previous studies (eg. by Mat-Isa et al., 2002, 2001, Li & Najarian, 2001, Mitra et al., 2000) analyse to determine the ability of the neural networks to diagnose cervical cancer were only done based on accuracy, sensitivity, specificity, false negative and false positive. The current study goes one step further by introducing analysis of confidence percentage and confidence level to analyse the degree of suitability of the HMLP network to be used as a cervical cancer diagnosis technique.

2. Hybrid Multilayered Perceptron Network

MLP network is a highly nonlinear neural networks. By using the MLP network, a linear system has to be approximated using the nonlinear neural network model. However, modelling a linear system using a nonlinear model can never be better than using a linear model. Therefore, Mashor in 2000, proposed additional linear input connections to the MLP network. The modified version of MLP is called hybrid multilayered perceptron (HMLP) network. As shown in Figure 1, the HMLP network allows the network inputs to be connected directly to the output nodes via weighted connections to form a linear model, which is in parallel with the nonlinear original MLP model.
As shown in Figure 1, for the HMLP network with \( m \) output nodes, \( n_h \) hidden nodes and \( n_i \) input nodes, the output of the \( k \)th neuron, \( y_k \), in the output layer is given by:

\[
\hat{y}_k(t) = \sum_{j=1}^{n_h} w^2_{jk} F \left( \sum_{i=1}^{n_i} w^1_{ij} x_i(t) + b^1_j \right) + \sum_{j=1}^{n_h} w^3_{jk} v_j(t)
\]

for \( 1 \leq k \leq m \) \hspace{1cm} (1)

where \( w^1_{ij} \), \( w^2_{jk} \) and \( w^3_{jk} \) denote the weights of the connection between input and hidden layer, weights of the connection between hidden and output layer, and weights of the linear connection between input and output layer respectively. \( b^1_j \) and \( v_j \) denote the thresholds in hidden nodes and inputs that are supplied to the input layer respectively. \( F(\bullet) \) is an activation function and is normally be selected as sigmoid function.

From Equation (1), the values of \( w^1_{ij} \), \( w^2_{jk} \), \( w^3_{jk} \) and \( b^1_j \) must be determined using appropriate algorithm. BP algorithm is commonly used to find optimum values for those parameters. Although the algorithm is easy to be implemented and produces a good performance, but its convergence rate is slow. To overcome the problems, Chen et al. (1990) proposed recursive prediction error (RPE) to replace the BP algorithm. The RPE algorithm provides a faster convergence rate and better final convergence values of weights and thresholds. In 2000, Mashor proposed a modified version of RPE algorithm, known as modified recursive prediction error (MRPE). By optimising the way the momentum and the learning rate are assigned, the MRPE algorithm is able to improve the convergence rate of the RPE algorithm. From the above discussion, the MRPE algorithm will be used to train the HMLP network in the current study.
The RPE algorithm modified by Chen et al. (1990) minimizes the following cost function:

\[ J(\hat{\Theta}) = \frac{1}{2N} \sum \overline{e}^T(t, \hat{\Theta}) \Lambda^{-1} \overline{e}(t, \hat{\Theta}) \]  

(2)

by updating the estimated parameter vector, \( \hat{\Theta} \) (consists of \( w_s \)s and \( b_s \)s), recursively using the Gauss-Newton algorithm:

\[ \hat{\Theta}(t) = \hat{\Theta}(t-1) + P(t)\Delta(t) \]  

(3)

and

\[ \Delta(t) = \alpha_m(t) \Delta(t-1) + \alpha_g(t) \psi(t) \varepsilon(t) \]  

(4)

where \( \varepsilon(t) \) and \( \Lambda \) are the prediction error and an \( m \times m \) symmetric positive definite matrix respectively, and \( m \) is the number of output nodes; \( \alpha_m(t) \) and \( \alpha_g(t) \) are the momentum and the learning rate respectively. \( \alpha_m(t) \) and \( \alpha_g(t) \) can be arbitrarily assigned to some values between 0 and 1, and the typical values of \( \alpha_m(t) \) and \( \alpha_g(t) \) are close to 1 and 0 respectively. In the present study, \( \alpha_m(t) \) and \( \alpha_g(t) \) are varied to improve further the convergence rate of the RPE algorithm according to:

\[ \alpha_m(t) = \alpha_m(t-1) + a \]  

(5)

and

\[ \alpha_g(t) = \alpha_m(t)(1 - \alpha_m(t)) \]  

(6)

where \( a \) is a small constant (typically \( a = 0.01 \)); \( \psi(t) \) represents the gradient of the one-step-ahead predicted output, \( y \) with respect to the network parameters:

\[ \psi(t, \Theta) = \left[ \frac{d y(t, \Theta)}{d \Theta} \right] \]  

(7)

\[ P(t) \] in equation (3) is updated recursively according to:

\[ P(t) = \frac{1}{\lambda(t)} \left[ P(t-1) - P(t-1)\psi(t) \right] \]  

(8)

where \( \lambda(t) \) is the forgetting factor, \( 0 < \lambda(t) < 1 \), and has been updated using the following scheme:

\[ \lambda(t) = \lambda_0 \lambda(t-1) + (1 - \lambda_0) \]  

(9)

where \( \lambda_0 \) and the initial forgetting factor, \( \lambda(0) \) are the design values. The initial value of the \( P(t) \) matrix, \( P(0) \) is set to \( \alpha I \) where \( I \) is the identity matrix and \( \alpha \) is a constant, typically between 100 and 10000.

The gradient matrix, \( \psi(t) \) can be modified to accommodate the extra linear connections for a one-hidden-layer HMLP network model by differentiating equation (1) with respect to the parameters, \( \theta_c \), to yield:

\[ \psi_k(k) = \frac{dy_k(t)}{d\theta_c} = \begin{cases} u_j & \text{if } \theta_c = w^2_{jk} 1 \leq j \leq n_k \\ x_i & \text{if } \theta_c = w^1_{ij} 0 \leq i \leq n_i \\ u_j (1 - u_j) w^2_{jk} x_i & \text{if } \theta_c = b_j 1 \leq j \leq n_k \\ u_j (1 - u_j) w^2_{jk} x_i & \text{if } \theta_c = w^1_{ij} 1 \leq j \leq n_k, 1 \leq i \leq n_i \\ 0 & \text{otherwise} \end{cases} \]  

(10)
The modified RPE algorithm for a one-hidden-layer HMLP network can be implemented as follows (Mashor, 2000):

1. Initialize weights, thresholds, \( P(0) \), \( a \), \( b \), \( \alpha_m(0) \), \( \lambda_0 \), and \( \lambda(0) \). \( b \) is a design parameter that has a typical value between 0.8 and 0.9.

2. Present inputs to the network and compute the network outputs according to equation (1).

3. Calculate the prediction error according to:
   \[ \varepsilon_k(t) = y_k(t) - \hat{y}_k(t) \] (11)
   where \( y_k(t) \) is the actual output.

4. Compute matrix \( \psi(t) \) according to equation (10). Note that, elements of \( \psi(t) \) should be calculated from the output layer down to the hidden layer.

5. Compute matrix \( P(t) \) and \( \lambda(t) \) according to equations (8) and (9) respectively.

6. If \( \alpha_m(t) < b \), update \( \alpha_m(t) \) according to equation (5).

7. Update \( \alpha_y(t) \) and \( \Delta(t) \) according to equations (6) and (4) respectively.

8. Update parameter vector \( \hat{\Theta}(t) \) according to equation (3).

9. Repeat steps (2) to (8) for each training data sample.

3. Confidence Percentage and Confidence Level Analysis

In most of the previous studies on diagnosis of cervical cancer using neural network, the suitability and the ability of the neural network to be used as a good cervical cancer diagnosis technique is determined solely based on accuracy, sensitivity, specificity, false negative and false positive. However, those five terms do not give clear picture on the strength or confidence level of the given diagnosis. Therefore, the current study introduced two new analysis techniques, known as diagnosis confidence percentage and diagnosis confidence level. The main purpose of introducing the two analysis is to give clearer picture on the strength or confidence level of each diagnosis.

In the current study, each output node will be assigned with either 0 or 10. Value 10 represents the type of cervical cells to be determined, while value 0 represents other type of cervical cell. Value 5 is the border value. If the output value is more than 5, the HMLP network will classify the cervical cells as the type of cervical cell to be determined, and if the output value is lower than 5, the network will classify the cervical cells as other type of cervical cell. From the explanation, if the output value is close to 0 or 10, so the HMLP network produce a strong diagnosis with high confidence level. But if the output value is close to 5, so the HMLP network produce a weak diagnosis with low confidence level. Therefore, the current study introduced diagnosis confidence percentage and diagnosis confidence level analysis to give a clearer picture on the strength and confidence level of each diagnosis, which is done by HMLP network.

Consider a case where \( H_a \) denotes the diagnosis of certain type of cervical cell (in the current study, \( H_a \) equals to 10) and \( H_b \) denotes the diagnosis of other type of cervical cell (in the current study, \( H_b \) equals to 0). \( H_s \) denotes the border value, calculated as:

\[ H_s = \frac{H_a + H_b}{2} \] (12)
The diagnosis confidence percentage can be determined by:

\[
\text{Confidence percentage} = \left\{ \begin{array}{ll}
\frac{100\%}{(H_a - H_b)/2} 
& \text{if } \hat{y} \geq H_a \\
\frac{\hat{y} - H_a}{H_a - H_b} \times 100\% & \text{if } H_a > \hat{y} > H_b \\
100\% & \text{if } \hat{y} \leq H_b
\end{array} \right.
\]  

(13)

where \( \hat{y} \) is the HMLP network predicted output.

For easier classification of diagnosis confidence level which is produced by the HMLP network, the diagnosis confidence level is proposed. The diagnosis confidence level is classified into five level (Level 1, 2, 3, 4 and 5) based on diagnosis confidence percentage as shown in Table 1. Diagnosis confidence Level 1, 2, 3, 4 and 5 denote highest, high, moderate, low and lowest confidence level respectively.

<table>
<thead>
<tr>
<th>Confidence level</th>
<th>Confidence percentage range</th>
<th>Confidence type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>80% to 100%</td>
<td>Highest</td>
</tr>
<tr>
<td>2</td>
<td>60% to 79%</td>
<td>High</td>
</tr>
<tr>
<td>3</td>
<td>40% to 59%</td>
<td>Moderate</td>
</tr>
<tr>
<td>4</td>
<td>20% to 39%</td>
<td>Low</td>
</tr>
<tr>
<td>5</td>
<td>0% to 19%</td>
<td>Lowest</td>
</tr>
</tbody>
</table>

4. Methodology and Data Samples

As mentioned above, HMLP network trained using MRPE algorithm is proposed as cervical cancer diagnosis technique. Cervical cancer has been classified in a variety of ways. The new and commonly used is the Bethesda system. Abnormal cervical cells are classified into two types; low grade intraepithelial lesions (LSIL) and high grade intraepithelial lesions (HSIL). Cytopathologists differentiate both types of abnormal cervical cells and normal cells based on several morphologies. The abnormal cervical cells show changes in nucleocytoplasmic ratio. The cytoplasm size decreases but the nucleus size increases from normal cells to HSIL cells through LSIL cells (Crum, 1994). This phenomena increase the nucleus-to-cytoplasm ratio. Besides that, the abnormal cervical cells also show changes in colour (grey level) of nucleus and cytoplasm (WebMD, 2002). The grey levels for the cells’ structures become darker from normal cells to HSIL cells through LSIL cells. Therefore, size of nucleus, size of cytoplasm, grey level of nucleus and grey level of cytoplasm will be used as inputs data for the HMLP network.

To determine the suitability of the HMLP network as cervical cancer diagnosis technique, the HMLP network needs to go through training and testing phase. During both phases, the optimum structure and diagnosis performance of the HMLP networks was determined. The analysis of diagnosis performance of the HMLP network is based on five important terms, which are accuracy, sensitivity, specificity, false negative and false positive. Accuracy is defined as the probability that the person is diagnosed correctly either positive or negative. Sensitivity refers to the probability that a symptom is present (or screening test is positive) given that the person has the
disease (occurrence of abnormal cells). Specificity is defined as the probability that a symptom is not present (or screening test is negative) given that the person does not have the disease (occurrence of normal cells). False negative refers to a person who was tested as negative who is actually positive while false positive refers to a person who was tested as positive who is actually negative. Beside that, the current study also introduce two new analysis techniques (as mentioned in the previous section) known as diagnosis confidence percentage and diagnosis confidence level analysis to determine the ability of the HMLP network to classify cervical cells. These two analyses will give clearer picture on strength and confidence level for each diagnosis, which is done by HMLP network.

In the current study, 200 cells (50 normal cells, 50 LSIL cells and 100 HSIL cells) were used in diagnosing cervical cancer using HMLP network. The data were taken from Hospital Universiti Sains Malaysia (HUSM). For each cell, four extracted features will be used as input data to the HMLP network, which are size of nucleus and cytoplasm and grey level of nucleus and cytoplasm. 128 data (32 normal cells, 32 LSIL cells and 62 HSIL cells) were used as training data while another 72 cells (18 normal cells, 18 LSIL cells and 36 HSIL cells) will be used as testing data.

5. Result and Discussion

The first step to determine the suitability of the HMLP network as cervical cancer diagnosis technique is to find the optimum structure of the network. In the current study, the HMLP network was trained using the following configuration:

\[
\alpha_n(0) = 0, \ \alpha_s(0) = 0.5, \ a = 0.01, \\
b = 0.85, \ \lambda_0 = 0.99, \ \lambda(0) = 0.95
\]

Note: Refer to MRPE algorithm in Section 2 for definition of these parameters.

Figure 2(a) and (b) show the diagnosis performance of HMLP network versus different number of epochs in the training and testing phase respectively. During the analysis, the number of hidden nodes is set to 10 hidden nodes. For every epoch in both phases, the HMLP network produced good diagnosis performance. The performance is maintained from 1 to 50 epochs. Both figures indicate that the HMLP network achieved its optimum diagnosis performance after it was trained for 5 epochs.

Determination of optimum hidden nodes of HMLP network is done based on the results shown in Figure 3(a) and (b). Figure 3(a) and (b) show the diagnosis performance of HMLP network during training and testing phase respectively. During the analysis, the HMLP network was trained for 5 epochs. From both figures, the diagnosis performance of HMLP networks are high and consistent. The HMLP network reached the optimum diagnosis performance after 10 hidden nodes were used.

![Fig 2(a) Training phase](image-url)
(b) Testing phase
Figure 2: Diagnosis performance of HMLP network for different number of epochs.

(a) Training phase
(b) Testing phase
Figure 3: Diagnosis performance of HMLP network for different number of hidden nodes.
After the HMLP network has been trained using MRPE algorithm, the result in Figure 2 and 3 show that the HMLP network needed 10 hidden nodes and 5 training epochs to produce optimum diagnosis performance. After the HMLP network has been properly trained, the HMLP network was tested using the training and testing data sets. The overall diagnosis result is shown in Table 2. The percentage of correct determination of normal, LSIL and HSIL cells are shown in Table 3. The result for diagnosis confidence level analysis for determination of normal, LSIL and HSIL cells are shown in Figure 4, 5 and 6 respectively. From these figures, 6 levels of diagnosis confidence are used. Level 1 to 5 denotes the proposed diagnosis confidence level, while Level 6 denote the case of incorrect cell determination.

The results in Table 2 indicated that the HMLP network gave good diagnosis performance. In the training phase, the HMLP network produced 96.09%, 94.79% and 100% of accuracy, sensitivity and specificity respectively, while in the testing phase, the HMLP network produced 94.44%, 92.59% and 100% of accuracy, sensitivity and specificity respectively. In both phases, the HMLP network produced low percentage of false negative and false negative rate. In the training phase, only 1.04% of false negative and 6.25% of false positive cases occurred, while in the testing phase, only 5.55% of false negative and 2.78% false positive cases occurred.

Table 2: Overall cervical cancer diagnosis result.

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Training phase</th>
<th>Testing phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accuracy</td>
<td>96.09</td>
<td>94.44</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>94.78</td>
<td>92.59</td>
</tr>
<tr>
<td>Specificity</td>
<td>100.00</td>
<td>100.00</td>
</tr>
<tr>
<td>False negative</td>
<td>1.04</td>
<td>5.55</td>
</tr>
<tr>
<td>False positive</td>
<td>6.25</td>
<td>2.78</td>
</tr>
</tbody>
</table>

Table 3: Percentage of correct determination of normal, LSIL and HSIL cells.

<table>
<thead>
<tr>
<th>Type of cell</th>
<th>Training phase</th>
<th>Testing phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal cells</td>
<td>100.00</td>
<td>100.00</td>
</tr>
<tr>
<td>LSIL cells</td>
<td>87.50</td>
<td>94.44</td>
</tr>
<tr>
<td>HSIL cells</td>
<td>98.44</td>
<td>91.67</td>
</tr>
<tr>
<td>Overall</td>
<td>96.09</td>
<td>94.44</td>
</tr>
</tbody>
</table>

The results in Table 3 showed that the HMLP network has superior ability to determine all normal cells correctly in both phases. The HMLP network also produced high percentage of correct determination for HSIL cells, which is 98.44% and 91.67% for training and testing phase respectively. The percentage of correct determination for LSIL
cells in the testing phase is also high, which is 94.44%. However, the percentage of correct determination for LSIL cells is slightly low in the training phase, which is 87.50%.

Overall, the results in Table 3 only give the percentage of correct determination for all type of cervical cells without giving a clear picture on the strength and confidence level of each diagnosis which was done by HMLP network. The strength and confidence level of diagnosis are shown in Figure 4, 5 and 6 for determination of normal, LSIL and HSIL respectively. From Figure 4, although the HMLP network can determine all normal cells correctly, but only 81.25% and 72.22% normal cells are determined with highest confidence level in training and testing phase respectively. In training phase, another 15.63% and 3.13% normal cells are determined correctly with high and moderate confidence level respectively. While, in the testing phase 11.11% and 16.67% normal cells are determined correctly with high and moderate confidence level respectively.

From Table 3, the HMLP network determined 87.50% and 94.44% LSIL cells correctly in the training and testing phase respectively. However, as shown in Figure 5, in the training phase, it is only about 50% LSIL cells are determined correctly with confidence level more than moderate and in the testing phase the percentage is lower, which is only about 40%. About 35% and 55% LSIL cells are determined correctly with low and lowest confidence level in the training and testing phase respectively.

On the other hand, the HMLP network can determine HSIL cells correctly with better confidence level as compared to LSIL cells as shown in Figure 6. In the training phase, 43.75%, 17.19% and 7.18% HSIL cells were determined correctly with highest, high and moderate confidence level respectively. Only 21.87% and 7.81% HSIL cells are determined correctly with low and lowest confidence level respectively. In the testing phase, 69.44%, 8.33% and 5.56% HSIL cells are determined correctly with highest, high and moderate confidence level respectively. Only 8.33% HSIL cells are determined correctly with low confidence level.

![Figure 4: Diagnosis confidence level results for determination of normal cells.](image)
6. Conclusion

The HMLP network trained using MRPE algorithm has been proposed to classify cervical cells into normal, LSIL and HSIL cells. Four features from Pap smear samples, which are size of nucleus, size of cytoplasm, grey level of nucleus and grey level of cytoplasm, have been used as HMLP network inputs data. From the result in the previous section, it has been proved that the HMLP network has successfully classified cervical cells with high accuracy, sensitivity and specificity, and low false negative and false positive. The HMLP has also successfully determined each type of cervical cells correctly with high percentage in both training and testing phase.

Two new analysis techniques namely diagnosis confidence percentage and diagnosis confidence level analysis have been introduced as diagnosis performance analysis techniques. Both analyses have been proved to give significant information about the strength and confidence level of each diagnosis which is done by HMLP network. From the confidence level analysis, the user will know either the diagnosis results can be accepted with or without confirmation by the
cytopathologist. The high confidence level indicates that the diagnosis result can be accepted without any doubt, while the low confidence level indicates that the diagnosis result must be confirmed by the pathologist.

References


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