PERFORMANCE OF IMAGE CYTOLOGY FEATURES VERSUS FOURIER TRANSFORM INFRARED SPECTROSCOPY (FTIR) FEATURES AS DIAGNOSIS INPUT FOR CERVICAL CANCER SCREENING TOOLS USING ARTIFICIAL NEURAL NETWORK

Nor Ashidi Mat Isa[1], Intan Aidha Yusoff [2], Yessi Jusman [3], Siti Noraini Sulaiman [4], Nor Hayati Othman [5]*

[1,2,3,4]School of Electrical & Electronic Engineering, Engineering Campus, Universiti Sains Malaysia, 14300 Nibong Tebal, Penang, Malaysia.
[5] Pathology Department, School of Medical Science, Medical Campus, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia.
*Correspondence to: Assoc. Prof. Dr. Nor Ashidi Mat Isa, Tel: +604-5996051, Fax: +604-5941023,
E-mail: ashidi@eng.usm.my

ABSTRACT

Statistically, 471,000 new cases of cervical cancer are reported in Malaysia each year, and more than 270,000 deaths were recorded. Cytology-based screening using Papanicolou (Pap) Test is the main screening method used currently for the secondary prevention of this silent killer. Unfortunately in Malaysia the screening coverage is very poor, which was at 2% in 1992, 3.5% in 1995, and at 6.2% in 1996 due to reasons including shortage of pathologist work force. In order to overcome this problem, numerous studies has been carried out, trying to turn the screening process into an automated system which is be able to give accurate result in shorter processing time compared to slide review process by pathologists. Two main fields which are researchers' favorite method and are known to be able of achieving such objective are through processing the cell's image cytology; and by studying the cervical solution compounds, by running thin prep solution through FTIR. Cell's image cytology process includes segmentation of regions and features extraction, such as grey level value, and cell's size. For FTIR, the criteria looked at the FTIR spectrums are such as areas under spectrum, height of compounds and slopes in certain frequency ranges. In this study, we used both features extracted from processing cell's image cytology and FTIR spectrums and tested them with two artificial neural network architecture, the Cascaded-MLP and Extreme Learning Machine. The features were used as input for neural network giving diagnosis of whether a sample is categorized into NORMAL, LSIL, or HSIL. The ability of each type of input data (image cytology versus FTIR spectrum) in determining correct diagnosis for samples is measured using accuracy performance. From the study done, it was observed that FTIR features extracted from cervical samples gave better accuracy when tested with neural network system in being a classifier tool for cervical cancer screening, compared to image cytology features tested with the same neural network architectures.

Keywords—*Cascaded Multilayer Perceptrons (c-MLP), Extreme Learning Machine (ELM), Cervical Cancer, Pap Smear.*

1. INTRODUCTION

Of all cancers amongst women worldwide, cervical cancer comprises 12% of it [1]. 273,000 patients died each year from 471,000 new cases diagnosed each year for cervical cancer, until 2007. For every two minutes one woman dies of this type of cancer [2]. Cervical cancer, especially invasive squamous cell carcinoma, is the second most prevalent cancer among women after skin cancer [3]. It is the most common cancer in many developing countries. There are over 370,000 new cases of cervical cancer each year, accounting for over 10% of cancers in women [4]. In United States of America, approximately 14,000 new cases of cervical cancer were diagnosed and over 5,000 women died each year, due to cervical cancer [5]. In Malaysia, cervical cancer constitutes 12.9% of cancer reported in women, putting it as second most type of cancer amongst women. 2000 to 3000 hospital admissions were recorded per year for cervical cancer. Cervical cancer progression may take many years for it to progress from pre-malignancy to invasive and or metastatic [6]. Hence, the incidence and mortality related to this disease can be significantly reduced through early detection and proper treatment.

Since the implementation of the Papanicolau (Pap) smear as a cancer-screening tool for the past 50 years, there has been dramatic decrease in both the incidence and mortality rates of cervical cancer [7].

Despite its success in reducing mortality from cervical cancer, the Pap test has several limitations; as in Malaysia, cervical cancer screening coverage is still poor, which stands at only 2% in 1992, 3.5% in 1995, and at only 6.2% in 1996 [8]. This situation is due to uneven distribution of medical facilities throughout the country, and shortage in pathologist workforce. Malaysia only has 242 pathologists in practice for a population of 25 million, which gives a ratio of 1:103,300 [8].

Numerous studies had been done to develop new automated screening system which can be used portably, without depending much on the workforce of pathologists, with the similar knowledge of interpreting data and giving out accurate results. One of the most famous approaches is by using neural network as classifier tool for features of cervical cells as input. This paper will focus on two most popular approaches of extracting features from cervical cells, which are Image Processing method, that is focusing on cytology features of the cells; and secondly FTIR which is used to study the structural changes of cells at the molecular level in term of spectral characteristics of cells and tissues in cervical cell samples. Studies done by Shady *et al* [9] and Fung *et al* [10] proved that FTIR could overcome the limitations exist in either standard Pap or Liquid Based Cytology (LBC) in terms of sensitivity, specificity, false-negative and false-positive rates.

This study concentrates on comparing the performance of these two methods of extracting features from cervical cells by looking at its individual performance when tested using two neural network architectures, Cascaded Multilayered Perceptron (c-MLP) and Extreme Learning Machine (ELM).

2. CELLS' CYTOLOGY AND COMPOSITION CHANGES

Both methods of Thin Prep Image Cytology and FTIR use difference in cell's appearance and composition to classify between Normal, LSIL (Low-Grade Squamous Intraepithelial Lession) and HSIL (High-Grade Squamous Intraepithelial Lession).

2.1. Cytological Changes

Cells which are infected with Human Papilloma Virus (HPV) that are developing into cancerous stage will show certain cytological changes which are:

i) Enlarged nucleus.

ii) Nucleus of abnormal cell (LSIL or HSIL) is much darker compared to normal cells.

2.2. Compound Changes

Spectral characteristics of cervical cells and tissue are results of carcinogenesis due to different modes of vibration in the molecules of the cells and tissues induced by Infra-Red lights. The difference between samples in cervical cells spectrum analysis is intensity of chemical compounds in certain wavelength, in which certain compound's intensity is to increase or decrease, such as glycogen and protein.

3. NEURAL NETWORK

Researchers worldwide had been using Artificial Neural Networks, ANNs as classifier tools because of its stability and ability to learn from examples and its capability for generalization beyond the training data [11]. It had been successfully used as classifier tools in various fields of studies such as signal and image pattern recognition and classification [12, 13, 14], financial forecasting [15] and medical diagnosis [16].

3.1. Cascaded Multilayered Perceptrons

For a single MLP network, equation for predicted output, y in the output layer is given by:

$$y = \varphi\left(\sum_{i=1}^{n} \quad\right) \quad \left(\quad^{T} \quad \right) \qquad (1)$$

Cascaded-MLP (c-MLP) architecture was developed by cascading several MLP networks together, as shown in [17].

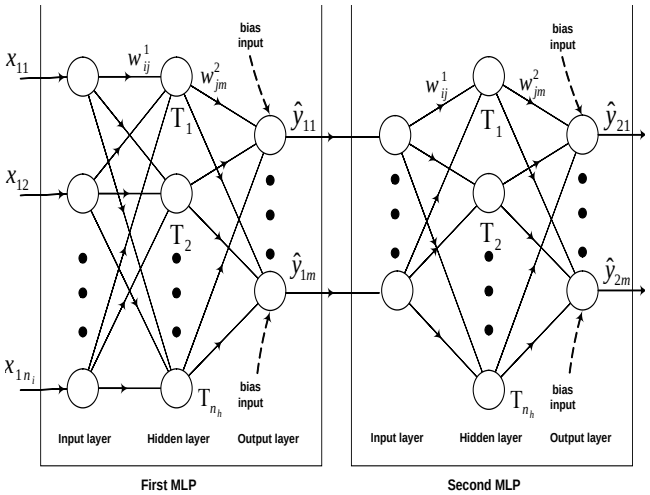

Figure 1. Structure of the c-MLP network

The c-MLP network is used in this study to classify the images into three types of diagnosis results: Normal, LSIL (low grade squamous intraepithelial lesions) or HSIL (high grade squamous intraepithelial squamous) cells.

All MLPs cascaded have the same initial setting. The number of nodes in hidden layers is determined manually by user. If the first MLP has 50 hidden nodes or being trained with 10,000 epochs, then the second held the same value of hidden nodes and epochs and so on [17]. Each succeeding MLP is employed to review and analyze the predicted outputs from the preceding MLP and give high priority for the misclassified samples [17]. C-MLP can increase a system's classification ability because if there were any feature of an input which was not recognized correctly, the second MLP will take up the task [17]. It has been proven in [17] that the three-cascaded MLP trained with Levenberg-Marquardt algorithm has better classification performance compared to several tested elarning algorithm in that study. Thus, the c-MLP trained with LM algorithm is used in this study. Further explanation on the c-MLP and the LM algorithm can be found in [15, 17].

3.2. Extreme Learning Machine

A new neural network algorithm named Extreme Learning Machine (ELM) has been developed for Single-Layer Feedforward Networks (SLFN) in [18, 19]. ELM had been successfully applied to many real world applications and has good generalization performance [20]. It was proven in [18,21], that for SLFNs with additive or RBF hidden nodes, the hidden node parameters may be randomly chosen and fixed to analytically determine the output weights when approximating any continuous target function.

ELM offers higher generalization performance than traditional gradient-based learning algorithms, has faster learning time and also avoids difficulties faced by gradient-based learning methods such as stopping criteria, learning rate, learning epochs, and local minima [18,21,22]. Basically, the algorithm tended to provide the best generalization performance at extremely fast learning speed. The new algorithm can produce best generalization performance in some cases and can learn much faster than traditional popular learning algorithms for feed-forward neural networks. The detailed description on ELM algorithm can be found in [18].

4. FEATURES EXTRACTION AND DATA PREPARATION

The features used as input to c-MLP and ELM neural network system are obtained in two different approaches, one being through image processing techniques, and another one is through FTIR processing.

4.1. Cytology Features Extraction

A set of data obtained from [23] are used as input to cascaded MLP and ELM based classifier system. The features are area of nucleus, area of cytoplasm, nucleus' grey level, cytoplasm's grey level, and red, blue, and green value of both nucleus and cytoplasm, Intensity1, Intensity2, and Saturation of nucleus and cytoplasm, which are computed using the following equations [23]:

$$Intensity1 = \frac{1}{3}(Red + Green + Blue) \quad (7)$$

$$Intensity2 = (Red)(0.299) + (Green)(0.587) + (Blue)(0.114) \quad (8)$$

$$Saturation = 1 - \frac{\sqrt{22}}{12}$$

$$c_1 = Red - 0.5 \times Blue \quad (9)$$

$$c_2 = \frac{\sqrt{3}}{2}(Green - Blue)$$

The images are captured from ThinPrep® slides using light microscope with embedded camera, at 40X magnification. The slides are obtained from Hospital Universiti Sains Malaysia (HUSM), Kelantan. 508 images of normal cervical cells, LSIL cells, and HSIL cells are captured with help from pathologists and lab technologists in HUSM. Sixteen (16) features are extracted from the images by using image processing system built with feature extraction algorithms [23].

4.2. FTIR Data Extraction

FTIR analysis results in an absorption spectrum which provides information about the chemical bonds and molecular structure of a material. The term Fourier Transform Infrared Spectroscopy refers to the manner in which the data is collected and converted from an interference pattern to a spectrum [24]. The FTIR spectrum is equivalent to the "fingerprint" of the material. FTIR Spectroscopy software is used for measuring and obtaining some significants characteristics of FTIR spectral. The frequency range used for analyzing between normal and abnormal samples, demonstrated in previous studies by [3], [7],

[9], [25]-[31], were approximately 1800-950 cm^{-1} in normalized spectra.

There are 8 proposed features to differentiate between normal and abnormal spectral. Figure 2 depicts the features mentioned below. The proposed features are;

i. area under spectrum at 1800-1500 cm^{-1},
ii. area under spectrum at 1200-1000 cm^{-1},
iii. area under spectrum at 1800-950 cm^{-1},
iv. height of slope at 1650-1550 cm^{-1},
v. corrected area of protein at 1590-1490 cm^{-1},
vi. corrected area of glycogen at 1134-985 cm^{-1},
vii. corrected peak height protein (H1545) and
viii. corrected peak height glycogen (H1045).

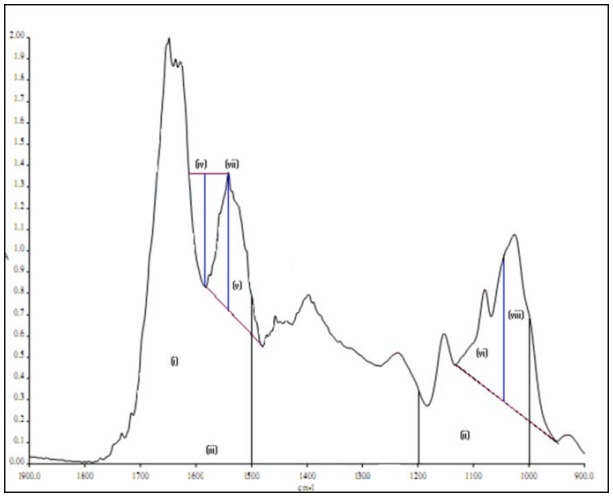

Figure 2. Fourier-transform infrared spectral changes of cervical cancer and the 8 features.

4.3. Training data and testing data

Data of each feature are divided into training and testing data with 80:20 ratio.
Four (4) sets of data with the same total of 508 data for cytology images and 176 data for FTIR are used and tested with the systems to observe systems' performance towards different data combination. The accuracy of each data set when tested using c-MLP and ELM algorithm are taken as result.

5. RESULT AND DISCUSSION

Table 2. Accuracy Result for c-MLP and ELM

Dataset	Accuracy	Cytology Images		FTIR Spectrum	
		Cascaded Multi Layered Perceptrons	Extreme Learning Machine	Cascaded Multi Layered Perceptrons	Extreme Learning Machine
Set1	Training	99.14	98.28	98.37	95.70
	Testing	95.10	92.16	95.28	96.70
	Average	**97.12**	**95.22**	**96.83**	**96.20**
Set2	Training	100.00	100.00	98.37	96.20
	Testing	92.65	89.22	95.28	95.70
	Average	**96.32**	**94.61**	**96.83**	**95.90**
Set3	Training	96.55	98.03	98.78	96.50
	Testing	93.63	92.16	95.28	94.60
	Average	**95.09**	**95.10**	**97.03**	**95.50**
Set4	Training	100.00	99.26	100.00	96.30
	Testing	95.54	89.11	96.23	94.80
	Average	**97.77**	**94.19**	**98.11**	**95.60**
AVERAGE		**96.58**	**94.78**	**97.20**	**95.80**

Overall performance shows that FTIR features combined with c-MLP architecture give the best accuracy of 97.20%, followed by c-MLP using Image Cytology features at 96.58%, then by FTIR features using ELM at 95.80%, and Image Cytology using ELM gives the lowest accuracy, with only 94.78%.

Generally both FTIR features and Image Cytology features give better results when tested using c-MLP architecture compared to ELM, proving that the c-MLP architecture provides better performance in term of accuracy of the system than ELM architecture.

This study is focusing on comparing between the performances of Image Cytology features versus FTIR spectrum features when used as diagnosis input for Artificial Neural Network as classifier tool. From the results gained, it is proven that FTIR gave better performance compared to Image Cytology, with average difference of 1% for each case.

6. CONCLUSION

This study proposed two neural network architectures, the Cascaded Multi Layered Perceptrons, and Extreme Learning Machine, to be used as classifier tools for screening activities on cervical cancer, with two types of features used as inputs to the system, cervical cells' image cytology captured from ThinPrep slides, and FTIR spectrum of cervical smear samples. Good performance of both type of features are seen as it both give an accuracy of >90%. The main objective of this study is to compare the performance between ThinPrep Image Cytology with FTIR spectrum features in being the input features of classifier tools for cervical cell images, and the result gained shows that FTIR features gave better accuracy when tested with both Artificial Neural Network architectures, with accuracy of 97.20% when used with c-MLP, and 95.80% when used with ELM. This is higher compared to ThinPrep Image Cytology with 96.58% and 94.78% for each type of classifier tool. Thus, it is proven that FTIR features extracted from cervical samples give better accuracy when tested with neural network system in being a classifier tool for cervical cancer screening, compared to image cytology features tested with the same neural network architectures.

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