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Image Processing to Quantitate Hemoglobin Level for Diagnostic Support

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Abstract
Digital Image processing techniques can be used to explore primitive diagnostics methods for disease detection at early stages with limited resources and skilled labor. These techniques can also assist doctors during clinical examination without any need for invasive pathological test and this facilitates patient comfort and avoids infection during blood test. Various blood components such as hemoglobin and billirubin whose approximate measure can directly be identified by just viewing the color of patient skin, nails, eye or any other target area can be measured and classified in terms of the color content of the image of the targeted area. Analysis of image processing techniques in conjunction with specialized supervision can provide significant exploration in the field of biomedicine and clinical applications. This research work proposes an image processing based non-invasive method of measuring hemoglobin (Hb) concentration present in patient's blood by analyzing the color and texture of digital photographs of patient's palpebral conjunctiva. The images of patient's palpebral conjunctiva were processed and eight relevant features were extracted .Artificial neural network classifier was used to correlate the output quantity to be measured with the values of the quantity measured by the standard method as per the guidelines given by WHO. Further, based on the testing results obtained by the classifier the patients whose Hb concentration was less than 11g/dL were screened as anaemic patients. A confusion matrix was then plotted to evaluate and compare the predicted classification results with the actual value of Hb obtained from invasive test. It was found that the proposed algorithm was able to diagnose anemia with 71.42% sensitivity and 89.47% specificity. The proposed method is helpful for detection of not only severe anemia but works well in detection of moderate anemia too thus predicting the hemoglobin value to an accuracy of 81.81%.The proposed work is useful for giving assistance to medical practitioners for reliable diagnosis of anaemia in the clinic itself and in low resource settings.

Keywords
Hemoglobin, Anemia, Palpebral Conjuctiva, Artificial Neural Network, Digital Image Processing

Introduction

Hemoglobin (Hb) is Metalloprotein containing iron which carries oxygen from lungs to organs via blood. The oxygen binding capacity of Hb is 1.34 ml O2 per gram. Decreased level of Hb intervene normal body functions and can hamper the health of an individual. Anemia is a condition in which the number and size of red blood cells or the hemoglobin concentration falls below an established cutoff value [2]. According to the statistics given by WHO the most common cause of anemia worldwide is iron deficiency which is approximately 50% [3]. WHO has given global nutrition targets 2025, achieving a 50% reduction of anemia in women of reproductive age [1]. Improving the identification, measurement and understanding of anemia and to monitor and evaluate the implementation of the control programs is under their action plans to re ach the targets [2]. The prevalence of anemia is highest in south Asia and central and west Africa[2]. Direct cyanmethemoglobin method is the gold standard for measurement of hemoglobin. Some other methods such as indirect cyanmethemoglobin, hemocue method also exists but most of these methods require well equipped clinical laboratories, commercial reagents and skilled technicians

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and labors which are most of the time not available in primary health care centers in rural areas. Hemoglobin color scale method is the method which can provide a practical solution in the developing countries for on field detection and management of anemia [4]. H. Ranganathan et al. [5] investigated by analyzing the color of glass slide prepared by smearing a drop of blood on it. The result showed a strong correlation between color of the glass slides and the actual Hb values of the subjects. All of the above methods are invasive in nature and needs drawing blood from a subject's body. Recent advances in Optical Imaging procedures and modalities have facilitated early diagnosis and treatment evaluation of critical diseases; these techniques include capturing a subject using a charged coupled device and fiber optics [6]. Noninvasive estimation of Hb using optical imaging technique which include studying the absorption spectra of hemoglobin species, analyze and reference wavelengths in visible and near infrared region is proposed by J. Todd Kuenster[7].George Zonios et al.[8] proposed technique to estimate skin melanin and hemoglobin using diffuse reflectance spectroscopy. Though these methods are non invasive in nature but they still need special sensors of specific wavelengths and skilled technicians which is again a limitation in rural areas. Physical diagnosis of anemia includes examination of pallor of conjunctiva, nail beds, tongue, palm and palmer creases. Ashwini kalantri et al. [9] evaluated the accuracy and reliability of pallor for anemia detection and found that presence of pallor can help detection of severe anemia but doesn't work well in detection of moderate anemia. Rebecca .J. Stoltzfus et al.[10] presented a study where they assessed usefulness of clinical pallor to detect severe anemia and concluded that clinical pallor was strongly associated with hemoglobin concentration and out of the different pallor sites conjunctiva pallor gives the best performance in terms of sensitivity and specificity. Although there are many studies indicating the correlation between clinical pallor and Hb values, the accuracy is not comparable to the gold standard. This is due to the poor inter-observer agreement which exists because each individual may have different color perception while examining the pallor site of the subject. This leads to poor accuracy and reliability of these methods Amalgamation of the traditional physical diagnosis of pallor and advanced digital processing and classification techniques may lead to faster, cost effective and reliable methods for estimating Hb concentration by processing images of pallor sites especially in rural areas. K.S. Srinivasan et al.[11] (200 suggested noninvasive detection of anemia by the color information derived by the photograph of the fingertip (typically thumb) taken first under standard conditions and later with occlusion of blood flow to the fingertip, using the same standard conditions. The mean RGB values of the input images were calculated and a multivariate regression analysis was carried out to find if there is a correlation between the difference in R, G and B values before and after applying pressure and the Hb value of the blood of the person. The relationship derived explains about 71% of the relationship that actually exists. Though the method is simple but the setup and the method to occlude the blood is not clear. Georgy D.Jay et al.[12] invented a non-invasive method of estimating Hb concentration by capturing digital image of a target area such as palpebral conjunctiva, nail beds, palm etc. along with a reference color card. The RGB color content of the target area and the reference card was analyzed and their ratio was calculated which resulted in measure of concentration of hemoglobin present in the blood. The reference card was used to avoid error in estimation of Hb due to the presence of ambient light conditions at the time of image acquisition. Though the method reduces the presence of ambient light still it is difficult to eliminate the color bias at the time of image acquisition as concluded by Shaun Collings et al.[13] in their proposed work .They have photographed conjunctiva using consumer camera along with in frame calibration card and determined the conjuctival erythema index EI and found a significant relation between palpebaral conjunctiva and Hb concentration with a sensitivity 69% and specificity 72% respectively.Vitoantonio Bevilacqua et al. [14] proposed development of an easy wearable device that patients themselves can employ at home to autonomously assess their need of blood transfusion. The model included Pi-Noir camera for image acquisition and Raspberry Pi for further processing. The extracted value of the images of conjunctiva were converted from RGB→CIE 1976 L*a*b* color scale and a* value was extracted which showed high correlation .A binary classifier was then trained which resulted in accuracy of (84.4%), specificity of (82.4%) and sensitivity (100%), thus making it possible to avoid a significant number of blood tests. C.C.Fan[15] extracted many color based features from the subjects palpebral conjunctiva images taken from common digital camera and correlated it with the actual Hb concentration of the subject.ANN and SVM were then trained out of which SVM outperformed giving sensitivity of 96.15% and specificity of 80%.Yi-Ming Chen et al.[16] proposed two algorithms for anemia diagnosis by processing color distribution of palpebral conjunctiva. The quick algorithm involved extraction of two color based features followed by classification resulting in sensitivity and specificity of 0.62 and 0.90 respectively. Total 18 features were extracted for the robust algorithm, followed by classification using ANN and SVM classifiers. The classification resulted in anemia screening with 78% sensitivity and 83% specificity using SVM classifier .During the literature survey it was found that the conventional methods used for detection of Hb are invasive in nature .Also non invasive methods for anemia detection were proposed by various researchers which are helpful for detection of severe anemia but doesn't work well for detection of moderate anemia. Hence the proposed research work was directed to develop a non-invasive and simpler method for measurement of Hb which can be viewed as an excellent alternative to the conventional methods and provide clinical support to clinicians for reliable diagnosis of diseases caused due to decreased level of Hb.

Methodology

This work aims to determine Hb concentration present in human blood by processing the images of palebral conjunctiva and the proposed approach i:s depicted in Fig.1.

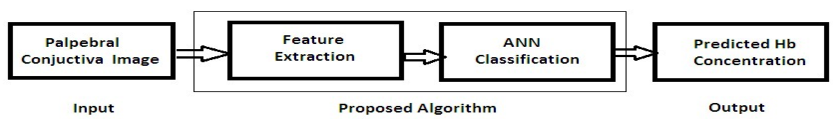

Fig 1: Block Diagram of Proposed Approach

The First stage receives the image of the palpebral conjunctiva of the subject taken from a normal camera whose Hb concentration is to be known. The second stage processes the image for compact representation by extracting the relevant features. Since the images may exhibit variations due to different causes including noise, template matching and correlation approach is unsuccessful. Also careful choice of invariant features to distinguish between different Hb levels is carried out. Logical investigation for the basis of discrimination of features is carried out and the extracted features are processed using intelligent machine learning algorithm to derive meaningful information for predicting the value of Hb concentration present in the subject's blood. The data set is partitioned into training and test set so as to enable the system to learn information which is then validated by test set. The experimentation data was provided by Dr. Ching-chao Fan from the Saint Mary's Hospital Luodog [15]. The data consists of an image which is a rectangular region cut from the palpebral conjunctiva image taken from a digital camera and the actual Hb concentration of subjects. Total 103 images and their respective Hb concentration values are provided.

Feature Extraction

Color distribution of palpebral conjunctiva is the standard procedure used for anemia diagnosis hence the original palpebral conjunctiva images are subjected to appropriate feature extraction process were eight different features based on color and texture are derived. These features include Mean R,G,B value(Rm,Gm,Bm) ,brightness(Brt),Erythema index (EI = log(Sred)-log(Sgreen));where Sred and Sgreen is the brightness of the image in the red and green channel respectively , a* value is extracted from CIE 1976 L*a*b* color scale as the positive a* values indicates the red component present in the image. As one of the important attributes of the CIE model is device independence which includes all perceivable colors and its gamut exceeds those of the other color models. Therefore this extra gamut is helpful for computer algorithms to make more precise calculations. Other two features namely high hue ratio (HHR) and Entropy are also extracted to characterize the texture of the image. HHR is given by the ratio of high hue pixels divided by the total number of pixel in the image. The image is first converted into HSV color scale and the mean hue of the image is calculated. A pixel is considered to be a high hue pixel if its hue is grater the mean hue value of the image and is thus useful in conditions where the illumination level varies. For calculating the entropy (Ent) statistical approach is used and the histogram equalization of the image is done after converting it into gray scale. The combination of color and texture features provides a robust feature set for Hb value prediction. The flowchart of the algorithm is as given below in fig.2

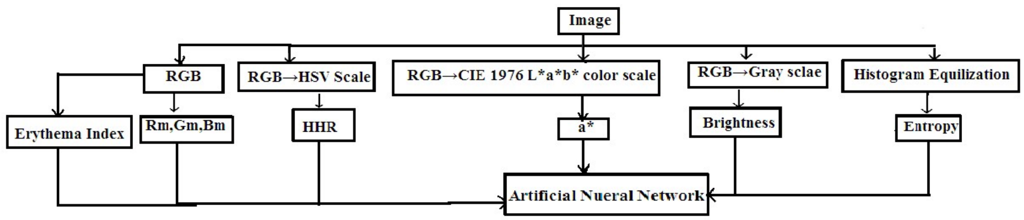

Fig. 2: Flow Chart of the Proposed Algorithm

Prediction of Hb Values

The palpebral conjunctiva images were processed and the extracted features formed the input to the artificial neural network. Out of the 103 samples available 70 samples were used to train the network and 33 samples were used for testing. The neural network used a single hidden layer network with eight nodes in the input layer and single node in the output layer. The final converged minimal network was trained with Levenberg Marquardt back propagation algorithm with best learning rate so as to determine weight change used for correction and it outperforms simple gradient descent and other conjugate gradient methods. The evaluation metric used was mean squared error. After extensive simulation based on input data distribution, the conclusion drawn is that using hyperbolic tangent sigmoid function the network converges with less number of computational nodes with respect to the resulting network errors. Also use of hyperbolic tangent sigmoid activation function in the hidden units, leads to no hidden layer unit becoming frozen and therefore the desired constraints are enforced on the output too.

Results

The results obtained after testing 33 samples for the proposed method are compared with the respective Hb value measured through laboratory test. Bland-Altman plot is plotted to compare the obtained results from the two methods. The plot is as shown in figure.3.The X axis indicates the mean of the measured values of Hb from the above mentioned two methods and Y-axis denotes the difference between the two measured values as a percentage of their average[17].

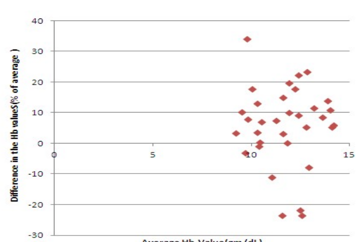

Fig. 3: Bland-Altman Plot

On the basis of results obtained out of 33 testing samples some essential statistical parameters were calculated using the formulae given in [18] and their values is indicated in table.1

Parameter	Calculated Value
Mean	12.02764
Variance	0.085477
Standard Deviation	0.292364
Coefficient of variance	2.430771

Table 1: Calculated Statistical Parameters

The 33 test samples included subjects with hemoglobin values ranging from 8-13.7g/dL. The performance and appropriateness of the proposed algorithm for detecting anemia is evaluated by plotting a confusion matrix as given in table.2 As the data does not include patients gender, age and sex the results for cutoff value of Hb is equal to 11 g/dL so that a subject having Hb concentration less than 11 is detected as anemic otherwise the patient is non-anemic.

	Actual Anemia	Actual non-anemia
Predicted Anemia	10 (TP)	2 (FP)
Predicted Non-anemia	4 (FN)	17 (TN)

Table 2: Experimental Results for Hb Cutoff 11 gm/dL

The sensitivity, specificity and accuracy of the above proposed algorithm are indicated in table.3 and these values are calculated as per the equations given in [18].

Performance Parameter	Value in percentage
Sensitivity	71.42
Specificity	89.47
Accuracy	81.81

Table 3: Performance of Proposed Algorithm

As mentioned in [18] in order to include the effect of inter observer agreement and quantify reliability of the method, kappa value, positive likelihood ratio and negative likelihood ratio are also evaluated and their calculated value is indicated in Table.4.

Discussions

It can be observed from Figure.3 that the difference cloud is clustered within 0% to +10%. It can be seen from table.1 that the coefficient of variance of the results obtained from the proposed algorithm is 2.43%.As reported in the manual for health workers for anemia detection methods in low resource settings [18] for a test to be acceptable for diagnosis the coefficient of variance should be less than 5%.It can be concluded that the test is acceptable as the obtained value of coefficient of variance of the proposed algorithm is less than 5%. The performance of the proposed algorithm is compared with the performance of the previous work done by C.C.Fan [15], Yi-Ming chen [16] and the standard non invasive test for detection of severe anemia based on clinical sign given by WHO [18] in table.4.

Parameter	Fan's work*	Yi-Ming chen et al work**	The proposed work***	Non-invasive method based on Clinical Signs as given WHO[18]
Sensitivity	0.74	0.78	0.71	0.64
specificity	0.83	0.83	0.89	0.70-1.00
LR+	6.2	4.65	6.78	-
LR-	0.42	0.25	0.32	-
Kappa Value	0.53	0.61	0.62	-

Table 4: Performance Comparison

* 43 testing sample with no cross validation,** 100 testing samples with 10 cross validation,***33 Testing samples with no cross validation

From table.4 it can be seen that the proposed system outperforms the work done previously in terms of specificity, positive likelihood ratio and kappa value. Since the severity of anemia is categorized by the hemoglobin concentration ranges, mild anemia and moderate is considered when hemoglobin value is between 7.0 -11 g/dl [18]. The results of experimentation indicate that all samples tested in the above mentioned range were correctly classified to an accuracy of 81.81%.Therefore the proposed algorithm and extracted features are suitable for detection of mild and moderate anemia too.

Conclusion

From the results obtained it can be concluded that the proposed minimal artificial neural network system can be used for assistance to medical practitioners for noninvasive detection of Hb at clinic itself. Above method can also be used for screening of anemia at lower resource setting. It is evident from the results that the sensitivity is in agreement to the specified values for screening anemia by using clinical signs [18] and specificity is higher than the specified by the other researchers indicating the extent to which a diagnostic test is specific for the experimental tested data. The proposed system is suitable for identifying mild and moderate anemia conditions. The strength of this study is the use of minimum features and its suitability to quantitate Hb Value followed by diagnosis of anemia in low resource clinical environment. The limitation includes image adjustment which may be due to the specific camera hardware or software. The performance of the algorithm can still be improved further by automatic disqualification and appropriate denoising of the input image due to the noise introduced by the ambient light conditions at the time of image acquisition. Further a low cost handheld device can be developed which can be used by health workers for on field Hb detection non-invasively.

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