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An Intelligent Method for Down Syndrome Detection in Fetuses Using Ultrasound Images and Deep Learning Neural Networks

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Keywords

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Abstract

Down syndrome (DS) is the most common genetic condition in the world and its early detection during the pregnancy has significant role for further assessments. Early intervention for infants and children with DS can make a major difference in improving their quality of life. This paper proposes an intelligent method for detection of Down syndrome in fetuses using ultrasound images and convolutional neural networks (ConvNet). Ultrasonography is a non-invasive way to diagnose DS. The important features in ultrasonography are Nuchal translucency, nasal bone, fetal heart rate, FMF angle, etc. Unlike the traditional methods, the proposed method doesn't need for any feature extraction. In the proposed method, ConvNet extract new effective feature automatically from ultrasound images. Also, particle swarm optimization (PSO) algorithm is used for optimal selection of ConvNet structure such as number of convolutional layers, number of pooling layers, learning rate and so on. The proposed method tested on Wisconsin University midwifery clinic and the obtained results showed that the proposed method has excellent performance in DS detection.

1. Introduction

Down syndrome is a condition in which a child is born with an extra copy of their 21st chromosome. Hence its other name is trisomy 21. Down syndrome is the most common Autosomal chromosome abnormality which occurs once in every 800-1000 infants [1]. Down syndrome can be analyzed at the earliest stage with the Nuchal translucency test. Down syndrome causes physical and mental developmental delays and disabilities. Many of the disabilities are lifelong, and they can also shorten life expectancy. However, people with Down syndrome can live healthy and fulfilling lives. Recent medical advances, as well as cultural and institutional support for people with Down syndrome and their families, provides many opportunities to help overcome the challenges of this condition [2, 3].

Screening test for Down syndrome consists of Blood test based methods and Ultrasonography-based methods. The blood test is performed in the first trimester to measure the proteins produced by Placenta Beta, HCG, and PAPP-A [4] and in the second trimester for triple and quadruple measures and AFP (alpha-fetoprotein) test. This will help to access the risk that the fetus is having any chromosomal abnormality. This blood test is no way harmful to the fetus. Unlike X-rays, gamma rays which cause radiation to the human body, medical ultrasound, also known as diagnostic sonography is the safest imaging technique with no side effects [5].

In recent years, extensive research have been done for early detection of Down syndrome using different tools. Conventionally, amniotic fluid cell culture and karyotype analysis have been widely used for prenatal diagnosis of Down's syndrome [6]. However, this method is time-consuming, usually taking over two weeks or longer to get results. In addition, amniotic fluid cell culture has a high rate of failure that limits its application in clinical diagnosis of Down's syndrome. Fluorescence in situ hybridization (FISH) is also used for prenatal diagnosis of Down's syndrome without the need of a cell culture. The FISH diagnosis results can be obtained within 24 h [7, 8]. However, FISH is cumbersome and labor-intensive, and requires extensive technical expertise. These drawbacks have limited its application for a large amount of clinical samples. Therefore, novel methods for rapid prenatal diagnosis of Down's syndrome with convenience, rapid and low labor intensity are needed.

With the rapid development of molecular biology and genome biology, a number of molecular approaches have been developed for the rapid identification of aneuploidy. Among these novel molecular approaches, quantitative fluorescent polymerase chain reaction (QFPCR) and

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multiplex ligation-dependent probe amplification (MLPA) were widely used in clinic diagnosis of genetic diseases caused by aneuploidy. These two approaches are highly accurate and robust, and allow processing of 96 samples at once in an automated system, with results being available in less than 48 h. However, both approaches are required to determine the fragment length of PCR products. The high cost of instruments and reagents of capillary electrophoresis limits the wide application of QF-PCR and MLPA in prenatal diagnosis of Down's syndrome [9- 11].

Quantitative real-time PCR (qPCR) does not require post-PCR steps or electrophoresis in the diagnosis of aneuploidy. The experiment is rapid and easy to conduct. It can be done automatically and the data are directly extracted from the real-time PCR machine, reducing the impact of subjective factors. The diagnosis results can be available within 3 h. In addition, dozens of specimens can be analyzed at the same time, which allows the test to be used in large-scale prenatal and neonatal screenings. The DSCR3 gene on chromosome 21 and the GAPDH gene on chromosome 12 are used in qPCR assay for relative quantification of gene copy number for the detection of Down's syndrome [12]. In this qPCR assay, two sets of primers were used to amplify two different fragments on the DSCR3 and GAPDH genes. Slight changes of annealing temperature or quality of template DNA can cause false negative or false positive results [13]. Therefore, selection of appropriate primers for consistent amplification efficiency is critically important for the sensitivity and specificity of aneuploidy identification.

According to the previous researches for automatic recognition of DS, there are two main aspects that should be considered during the design of recognizer. One of these issues is the feature extraction and feature selection. Based on the investigated papers, it is witnessed that using new features as the input of classifier have led to better performance. Another issue is related to the type of classifier. In most studies, ANN, SVM, and ANFIS are used as the classifier. The most common and useful training algorithm for ANNs is the BP algorithm, that uses gradient information for finding the unknown weights and biases. Gradient-based algorithms easily get trapped in local minima notably for nonlinear and complicated pattern recognition problems. In addition, the convergence speed of gradient-based algorithms is very low even for simple pattern recognition problems. Also, there is not any standardized approach to choose the neural network's architecture. Generally, it is required to obtain this architecture empirically, which is a time-consuming process [14- 17]. About the SVM, its accuracy is dependent on the selection of the kernel function and other parameters such as slack variables, cost parameter, and the margin of the hyperplane. There is a direct relationship between the failure in finding the optimal settings for an SVM model and its recognition accuracy. The computational cost of the SVM is another barrier [18- 22]. About the fuzzy systems, the error rate of fuzzy systems is high as they suffer from the necessity of large training data set and problems of random initial cluster center selection [23].

All the presented methods for DS recognition so far, demand the signal preprocessing, handcrafted features extraction and feature selection. The conventional techniques have acceptable performance, but they are very complicated and have several modules. In these systems, features are usually chosen using the trial-and-error or even by the experience. Therefore, we applied a convolutional neural network (ConvNet) in this paper to overwhelm the possible problems while using the traditional methods and also to acquire better detection accuracy without using any handcrafted feature extraction, feature selection features. In the proposed method, the particle swarm optimization (PSO) algorithm is used for optimal tuning of ConvNet parameters.

The rest of this paper is established as follows: Section 2 represents ConvNet. Part 3 is about the optimization algorithm. In part 4, we presented the proposed method. Section 5, is the simulation results, and finally, part 6 is the conclusion.

2. ConvNet

The ConvNets are one of the newly introduced and useful machine learning tools which have excellent performance in different applications like pattern recognition and fault detection. A ConvNet consists of three sorts of main layers, containing pooling layer (Pool), convolutional layer (CONV), and fully-connected layer. The main structure of the ConvNet is shown in Figure 2. The ConvNet in Figure 2 has one CONV layer, one Pool layer, and one fully connected layer. The number of CONV and Pool layers or hidden layers can be more than one. The user should select the optimal number of hidden layers.

In CONV layer, some convolution kernels have been utilized to calculate new feature maps [24]. The value of each feature at the location (i, j) in the k-th feature map of the l-th layer, $z_{i,j,k}^{l}$ is given as Eq. (1)

$$z_{i,j,k}^{l} = W_k^{l^T} X_{i,j}^{l} + b_k^{l} \quad (1)$$

In Eq. (1), W_k^l represent the weight vector and b_k^l denotes the bias term of the k-th filter of the l-th layer, and $X_{i,j}^l$ shows the input patch centered at the position $(the\ i, j)$ of the l-th layer. The activation value $a_{i,j,k}^l$ of convolutional feature $z_{i,j,k}^l$ is given by Eq. (2)

$$a_{i,j,k}^{l} = a\left(z_{i,j,k}^{l}\right) \quad (2)$$

where $a(.)$ is the activation function with the nonlinearity characteristic. Among several activation function types, the Rectified Linear Unit (ReLU) is one of the most effective and well-known activation function which can be defined as Eq. (3)

$$a_{i,j,k}^{l} = \max\left(z_{i,j,k}^{l}, 0\right) \quad (3)$$

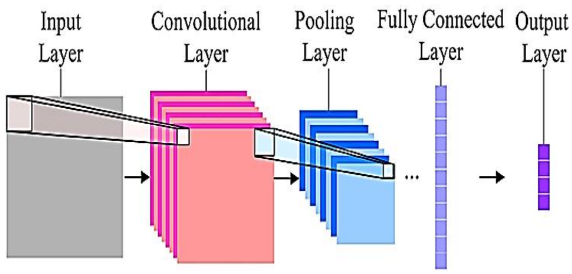

Figure 1. The main structure of the ConvNet

A possible drawback of the ReLU activation function is that, whenever the unit is not active, it has zero gradients . Consequently, the training process will be slow because of the constant zero gradients. In [25] a new model of activation function called Exponential Linear Unit (ELU) is proposed to allow the faster learning procedure of ConvNet which results in better performance. Similar to ReLU, in ELU the vanishing gradient problem can be prevented properly by tuning the positive part of identity. Unlike the ReLU, there is a negative part in ELU to make the learning process fast. To lessen the units' variation while deactivated and make a robust ELU against noise, it is required to apply a saturation function as the negative part besides the unsaturated negative parts. The ELU is given by Eq. (4)

$$a^{l}_{i,j,k} = \max\left(z^{l}_{i,j,k}, 0\right) + \min(\lambda(e^{z_{i,j,k}} - 1), 0) \quad (4)$$

In this equation, λ is a free parameter that controls the saturation of ELU for negative inputs. Considering the advantages of the ELU activation function, the ELU has used in the proposed method for CCPs recognition.

Shift-invariance in the pooling layer can be acquired using diminishing the feature maps resolution. The Pooling layer lies between two CONV layers. The pooling function can be symbolized as $pool\,(.)$, for each feature map $a^{l}_{i,j,k}$ which is given as Eq. (5)

$$y^{l}_{i,j,k} = \text{pool}\left(a^{l}_{m,n,k}\right), \forall (m,n) \in R_{ij} \quad (5)$$

In Eq. (5), R_{ij} is a local neighborhood around the location (i,j). The common pooling operations are L2-norm pooling, average pooling and, max pooling. After one or more hidden layer including CONV/Pool layers, there are fully connected and an output layer. The fully connected layer takes the extracted features by hidden layers and make a linear relationship between these new inputs and targets. Softmax is a popular used operator, especially for pattern recognition problems. Minimizing a suitable loss function which is defined on a particular task, makes it possible to get its optimum parameters(θ). If there exists N input-output relations $\left\{\left(x^{(n)}, y^{(n)}\right); n \in [1,2,\dots,N]\right\}$, where $x^{(n)}$ is the $n-$th input data, $y^{(n)}$ is its target label correspondingly and $o^{(n)}$is the output of ConvNet. The loss of ConvNet can be stated as Eq. (6)

$$\ell = 1/N \sum_{n-1}^{N} \ell\left(\theta : y^{(n)}, o^{(n)}\right) \quad (6)$$

The training of ConvNet is a nonlinear and complicated optimization problem. To get the best fitting set of the parameters including the weights and biases, we should minimize the loss function. The common solution for optimizing the ConvNet network is Stochastic gradient descent [25].

3. PSO

In the few past decades, nature-based optimization algorithms have been applied for different engineering problems [26- 32]. One of the most effective algorithms is PSO. The basic operational principle of the particle swarm is reminiscent of the behavior of a group, for example, a flock of birds or school of fish, or the social behavior of a group of people. Each individual flies in the search space with a velocity which is dynamically adjusted according to its own flying experience and its companions' flying experience, instead of using evolutionary operators to manipulate the individuals like in other evolutionary computational algorithms. Each individual is considered as a volume-less particle (a point) in the N-dimensional search space. At time step t, the ith particle is represented as: $X_i\,(t) = \left(x_{i1}\,(t), x_{i2}\,(t), \dots, x_{iN}(t)\right)$.The set of positions of m particles in a multidimensional space is identified as $X = \left\{X_l, \dots, X_j, \dots, X_i, \dots, X_m\right\}$.The best previous position (the position giving the best fitness value) of the ith particle is recorded and represented as $P_i\,(t) = (P_{i1}, P_{i2}, \dots, P_{iN})$. The index of the best particle among all the particles in the population (global model) is represented by the symbol g. The index of the best particle among all the particles in a defined topological neighborhood (local model) is represented by the index subscript l. The rate of movement of the position (velocity) for particle i at the time step t is represented as $V_i\,(t) = \left(V_{i1}\,(t), V_{i2}\,(t), \dots, V_{iN}(t)\right)$.The particle variables are manipulated according to the Eq. (7) (global model [33]):

$$\begin{aligned} V_{in}\,(t) = {} & W_i * V_{in}\,(t-1) + C_1 * rand1\,(.) \\ & * \left(P_{in} - X_{in}\,(t-1)\right) + C_2 \\ & * rand2\,(.) * \left(P_{gn} - X_{in}(t-1)\right) \end{aligned} \quad (7)$$

$$X_{in}(t) = X_{in}\,(t-1) + V_{in}\,(t)$$

where n is the dimension . $(1 \le n \le N)$, $C_1$and C_2 are positive constants, $rand1\,(.)$ and $rand2\,(.)$ are two random functions in the range [0,1], and W is the inertia weight. For the neighborhood ($lbest$) model, the only change is to substitute P_{ln} for P_{gn} in the equation for velocity. This equation in the global model is used to calculate a particle's new velocity according to its previous velocity and the distance of its current position from its own best experience ($pbest$)and the group's best experience($gbest$). The local model calculation is identical, except that the neighborhood's best experience is used instead of the group's best experience. Particle swarm optimization has been used for approaches that can be used across a wide range of applications, as well as for specific applications focused on a specific requirement. Its attractiveness over many other optimization algorithms relies in its relative simplicity because only a few parameters need to be adjusted.

4. Proposed Method

The current procedure assumes that the ultrasound image is recorded that it is interpreted by a human expert. Obviously, this suffers from the human error and error with visual inspection, which may further be enhanced by poor quality of the images. This paper proposes an intelligent system based on combination of ConvNet and PSO for Down Syndrome diagnosis. The ConvNet has performed relatively well on image processing and pattern recognition. The proposed method includes two main modules: classifier module and optimization module. In the classifier module, ConvNet is used as the main classifier.

In the proposed method, the raw data is fed to ConvNet layer to extract new features. The features extracted from the convolution and pooling process were broken down into sequential components and fed to the fully connected layer for caries recognition. There are many parameters and hyper-parameters that affect the network's performance significantly. The amount of unknown parameters will increase dramatically with the increase of hidden layer numbers and there are no systematic way to find the optimal value of these unknown parameters and hyper-parameters. To overcome this problem, we have proposed an intelligent method based on PSO to find the optimal architecture of the CNN. The main structure of the proposed method is shown in Figure 2.

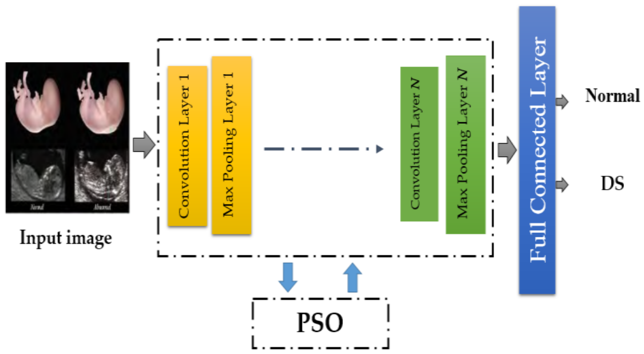

Figure 2. The main structure of the proposed system

One of the key issues in evaluating the performance of a classification approach is the capability of correct classification of new examples. The classification performance of two class problems can be interpreted in a confusion matrix as shown in Table 1.

Table 1. Confusion matrix

Data class	Classified as positive	Classified as negative
Positive	TP	FN
Negative	FP	TN

The entries in the confusion matrix have the following meaning in the context of our study:

TP is the number of correct predictions that an instance is positive.

FN is the number of incorrect predictions that an instance is negative.

FP is the number of incorrect predictions that an instance positive.

TN is the number of correct predictions that an instance is negative.

The most commonly used measure to evaluate the performance of a classifier is recognition accuracy (RA) rate. The RA is the proportion of the total number of predictions that were correct to all samples as defined by the Eq. (8)

$$\mathrm{RA} = \frac{\mathrm{TP} + \mathrm{TN}}{\mathrm{TP} + \mathrm{FN} + \mathrm{FP} + \mathrm{TN}} \times 100 \tag{8}$$

5. Simulation Result

In this section the performance of the proposed method is investigated. The computational experiments for this section were done on Intel core i7 with 32 GB RAM using ASUS computer. The proposed method tested on Wisconsin University midwifery clinic. This dataset contains 300 images which 171 of them are related to DS and the 129 samples are related to normal fetuses. In this study, 40% of data were used in order for training the classifiers and the rest for testing. All the mentioned results in this paper is the average of 50 independent runs.

5.1. Performance of the Conventional ConvNet

In this experiment, the effect of parameters and hyper-parameters on ConvNet performance is investigated. For this purpose, several ConvNet with different architecture have been built and the obtained results are listed in Table 2. It can be seen that the ConvNet with three hidden layer and Max Pooling functions in POOL layer has the best recognition accuracy. Based on Table 2 we can conclude that the architecture of ConvNet has high effect on its accuracy and its robustness. The value of standard deviation (SD) for different architectures are listed in the table. In order to indicate the details of the recognition for each pattern, the confusion matrix of recognizer is shown by Table 3.

Table 3. Confusion matrix of conventional ConvNet for the best obtained result

	Normal	DS
Normal	82	2
DS	2	92

Table 2. Evaluation of CNN with different architecures

NHL	a	TPL	Hyper-parameters	RA (%)	SD
1	0.01	Max	$K_{1C}=10, F_{1C}=4, S_{1C}=1, P_{1C}=1, F_{1P}=5, S_{1C}=1$	88.75	± 1.19
1	0.005	Max	$K_{1C}=10, F_{1C}=4, S_{1C}=1, P_{1C}=1, F_{1P}=5, S_{1C}=1$	91.25	± 1.14
2	0.005	Max	$K_{1C}=10, F_{1C}=4, S_{1C}=1, P_{1C}=1, F_{1P}=5, S_{1C}=1$ $K_{2C}=12, F_{2C}=3, S_{2C}=1, P_{2C}=1, F_{2P}=3, S_{2C}=1$	96.31	± 0.81
2	0.005	average	$K_{1C}=10, F_{1C}=4, S_{1C}=1, P_{1C}=1, F_{1P}=5, S_{1C}=1$ $K_{2C}=14, F_{2C}=3, S_{2C}=1, P_{2C}=2, F_{2P}=2, S_{2C}=1$	96.18	± 0.87
3	0.005	Max	$K_{1C}=10, F_{1C}=4, S_{1C}=1, P_{1C}=1, F_{1P}=5, S_{1C}=1$ $K_{2C}=12, F_{2C}=3, S_{2C}=1, P_{2C}=1, F_{2P}=3, S_{2C}=1$ $K_{3C}=18, F_{3C}=3, S_{3C}=1, P_{3C}=1, F_{3P}=3, S_{3C}=1$	97.18	± 0.49
3	0.005	L2-norm	$K_{1C}=10, F_{1C}=4, S_{1C}=1, P_{1C}=1, F_{1P}=5, S_{1C}=1$ $K_{2C}=14, F_{2C}=3, S_{2C}=2, P_{2C}=2, F_{2P}=2, S_{2C}=1$ $K_{3C}=24, F_{3C}=3, S_{3C}=1, P_{3C}=1, F_{3P}=3, S_{3C}=1$	96.87	± 0.53

5.2. Performance of the Proposed Method

In this experiment, the performance of the proposed method has been investigated. Deep learning architecture is represented by parameterized functions and hence the optimal parameters have direct impact on its accuracy. In order to find out the optimal values of these parameters and hyper-parameters, we used PSO as the optimization algorithm. The PSO should find the best parameters and hyper-parameters of the ConvNet to enhance the RA rate. Table 4 shows the PSO control parameters.

Table 4. PSO control parameters

Number of particles (n)	30
C1	1.8
C2	2
Initial weight	4
Number of iterations	100

The obtained results using the proposed method is listed in Table 5. Based on PSO, the ConvNet with four hidden layer, learning rate 0.0037 and Max Pooling function in POOL layer has the best recognition accuracy, 99.38%. The confusion matrix of the proposed method is shown by Table 6. It can be seen that the correct RA rate has increased significantly. The SD of the proposed method is zero (SD = $\pm$0.0).

Table 5. Performance of the proposed method and the proposed architecture

Layer	K	F	S	P
0	-	-	-	-
1st CONV	16	24×24	1	1
1st POOL	16	16×16	2	-
2nd CONV	28	20×20	1	1
2nd POOL	28	11×11	2	-
3rd CONV	60	16×16	1	2
3rd POOL	60	8×8	2	-
4th CONV	112	6×6	1	1
4th POOL	112	3×3	1	-
5th CONV	158	4×4	1	1
5th POOL	158	2×2	1	-

Table 6. Confusion matrix of the proposed method

	Normal	DS
Normal	84	0
DS	1	93

5.3. Comparison with Different Classifiers

In this experiment, the performance of the proposed method has been compared with other classifiers. In this respect, probabilistic neural networks (PNN), Multi layered Perceptron (MLP) neural network with different training algorithm such as Back propagation (BP) learning algorithm, Resilient propagation (RP) learning algorithm and Levenberg Marquardt (LM), Radial Basis Function Neural Network (RBFNN), Adaptive Neuro-Fuzzy Inference System (ANFIS) are considered. In this experiment, we used raw data as the input of the classifiers. It can be seen from Table 7 that the proposed method (PSO-ConvNet) has much better performance in comparison with other methods. Also the proposed method has robust performance.

Table 7. Comparison the performance of proposed classifier with other classifiers using raw data

Classifier	RA (%)	SD
PNN	93.26	$\pm$2.16
MLP (BP)	91.43	$\pm$3.70
MLP (RP)	95.24	$\pm$1.43
MLP (LM)	96.17	$\pm$1.28
RBFNN	96.62	$\pm$1.21
ANFIS	96.81	$\pm$0.78
Proposed method	99.38	$\pm$0.0

6. Conclusion

Down syndrome or Trisomy 21 is a chromosomal disorder which causes birth defects and mental retardation. Chromosomal disorders are detected using invasive and noninvasive testing. Ultrasound scan which is a noninvasive test and an improved methodology to identify pregnancies at increased risk of chromosomal abnormalities and Down Syndrome. In this study a new method based on intelligent combination of ConvNet and PSO proposed for automatic diagnosis of DS. Several experiments were performed to evaluate the performance of the proposed method and the obtained results showed that the proposed method has better performance in comparison with other methods. The proposed hybrid system of ConvNet and PSO model has delivered promising results as compared to the other conventional studies. In the proposed method, feature extraction and selection techniques are not required.

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