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Development of a neural network screening aid for diagnosing lower limb peripheral vascular disease from photoelectric plethysmography pulse waveforms

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Abstract. An artificial neural network (ANN) was trained to classify photoelectric plethysmographic (PPG) pulse waveforms for the diagnosis of lower limb peripheral vascular disease (PVD). PPG pulses from the lower limbs, and pre- and post-exercise Doppler ultrasound ankle to brachial systolic blood pressure ratio measurements were obtained from patients referred to a vascular investigation laboratory. A single PPG pulse from the big toe of each leg was processed and normalized, and used as input data to the ANN. The ANN outputs represented the diagnostic classifications (normal, significant PVD and major PVD) and the ANN was trained with the ankle to brachial pressure indices (ABPI). The ANN structure consisted of an input layer (50 neuron units from the PPG pulse input), a single hidden layer (15 neurons) and an output layer (3 neurons for the PVD diagnoses). The back-propagation learning algorithm was used to train the ANN for 500 epochs with a PPG training set of pulses from 100 legs. Test data for network assessment comprised pulses from a further 50 legs (20 normal and 30 PVD, of which 15 were categorized as having major disease). A network sensitivity of 93% and specificity of 85% was achieved with respect to the Doppler ABPI standard, giving a diagnostic accuracy of 90%. The results of this study indicate that a neural network can be trained to distinguish between PPG pulses from normal and diseased lower limb arteries. The simplicity of PPG measurement and neural network classification holds promise for the screening of lower limb arterial PVD.

1. Introduction

1.1. Arterial function in health and disease

The systemic arterial system is a complex network of branching elastic tubes which distribute blood from the heart, and at its multiple terminations passes blood on into the arterioles and capillaries of the organs and tissues of the body (Nichols and O'Rourke 1990). Trauma or disease may cause impairment or even failure of this finely regulated control system. Peripheral vascular disease (PVD) can affect both upper and lower limbs and is relatively common, especially in the western world, it affects both arteries and veins, although it is disease of the arteries which draws more attention.

In the peripheral circulation, atherosclerosis (Hertzer 1991) of increasing severity leads progressively to intermittent claudication (exercise-induced pain), rest pain, and tissue damage in the form of ischaemic ulceration or gangrene. A limb with rest pain or tissue damage is considered to be critically ischaemic since, without intervention to improve the circulation to the limb, there is a risk of limb loss and, without amputation,

death. Even milder degrees of atherosclerosis can interfere significantly with the lifestyle and well-being of patients, particularly in younger, active patients whose employment may be compromised. Although around three-quarters of patients with PVD have stable symptoms, from five to ten per cent may require amputation. It is therefore important to establish the exact cause of a patient's symptoms given that other conditions, including musculoskeletal disease, spinal disease, and venous disease, may produce similar symptoms.

There are several established diagnostic screening tests (AbuRahma 1988) for PVD which supplement the conventional clinical examination of patient history, auscultation and palpation. Frequently used non-invasive techniques include Doppler ultrasound, stress testing, segmental blood pressure measurement and plethysmography. Invasive techniques include angiography and nuclear medicine imaging. Each of these tests provides valuable information but unfortunately no single one is ideal. Ideally, a diagnostic test should be quick, practical, simple, non-invasive and accurate. This paper investigates the accuracy of photoelectric plethysmography (PPG) as a screening aid, since the technique is non-invasive and quick and easy to use. The pulse waveform derived from the technique has in the past been difficult to classify and so we therefore explored the use of a ANN for this classification.

1.2. Photoelectric plethysmography

The PPG technique (Jago and Murray 1988) utilizes an optical transducer which produces a signal associated with the change in volume of red blood cells in the peripheral micro-vascular bed with each pressure pulse initiated by the heart. In arteries having occlusive disease, the arterial resistance is increased, producing pulse waveforms which are characteristically different from those in normal subjects, and this can 'stretch' or 'flatten' normal pulsatile waveforms (Nichols and O'Rourke 1990). An example from one patient showing the difference in waveform shape between the left leg, having mild to moderate PVD, and the right leg, having major PVD, is illustrated in Figure 1.

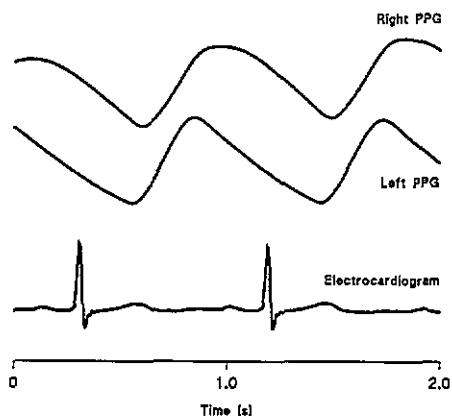


Figure 1. Photoelectric plethysmographic waveforms from a patient. Note that there is greater disease in the right leg. Both pulses are however more rounded than those recorded in normal subjects.

The pulse pick-up transducer usually consists of two photodiodes, one for transmission and the other for receiving reflected light. The transducer converts the optical signal into an electrical signal suitable for amplification and signal processing.

The operating wavelength can vary but is often in the near infrared region close to the isobestic point of 805 nm. This wavelength is used because the effect of different oxyhaemoglobin saturation levels is reduced.

1.3. Artificial neural networks

In neural computing (Willis *et al* 1990), mathematical processing units (neurons) are linked together by weighted connections. Each neuron processes its weighted inputs according to its activation function, and its output is then connected to the inputs of the next layer of neurons. Networks usually have a non-linear activation function, of which a popular choice is the logistic (sigmoidal) activation function. By allocating appropriate values to the weights, an ANN can perform complicated operations on its inputs. A network can be trained to perform a particular operation using a set of training data comprising a series of input patterns for which the correct output is known. Each training pattern is presented to the inputs in turn. The network weights, originally set to random values, are then optimized using a training algorithm. Training continues until the errors associated with the training set are minimized. Neural networks can solve classification problems when the input data is difficult to describe, and therefore hold promise for medical applications.

In this paper, the network was trained using the back-propagation method (McClelland and Rumelhart 1988) to distinguish between pulses from legs which are normal or have significant or major PVD. Back-propagation was chosen because it is relatively simple, well known and easy to implement. In addition to pulse classification, the effect of changing training parameters (learning rate and momentum) on network performance was investigated.

1.4. Aim

The aim of the study was to determine the accuracy of using PPG pulse waveforms to classify PVD of the lower limb arteries, using a neural network to compute the classification.

2. Methods

2.1. Patients

All measurements were performed in a vascular measurement laboratory during routine clinical investigations. In order to stabilize cardiovascular parameters and so standardize measurement conditions every patient rested in a supine position for a period of at least 5 min before commencement of physiological measurements.

Some patients were excluded from this study, including those having diabetes mellitus, cardiac arrhythmias, lower limb tremor, previous lower limb vascular surgery, and inability to attempt the treadmill exercise test. During the time of the study, approximately 25% of the patients referred for investigation were not included for the above reasons. Suitable recordings were obtained from a total of 150 legs which formed the basis of this study.

2.2. Doppler ultrasound studies for network reference data

Arterial disease was classified using pre- and post-exercise systolic blood pressure measurements which were obtained using a sphygmomanometer and a Doppler ultrasound probe to detect arterial blood flow. Systolic blood pressures were measured non-invasively in the upper limbs (highest of left- or right-side brachial systolic pressure, BSP) and in the lower limbs (ankle systolic pressure ASP, the highest of dorsalis pedis or posterior tibial arteries). The order of measurements before exercise was right arm, left arm, right leg and left leg; post-exercise pressure measurement order was most symptomatic leg, least symptomatic leg, right arm and finally left arm. Measurements were made using continuous wave (cw) Doppler ultrasound (Sonicaid, type Vasoflo IIC).

The ankle/brachial pressure index (ABPI) (Yao *et al* 1969) is defined as the ratio of ASP to BSP. This index is usually close to 1 for normal healthy subjects and less than 1 for patients who have significant PVD (Kester and Leveson 1981). To further quantify the functional impairment of patients with claudication, the response of the ASP and BSP to constant-load treadmill exercise may be determined. The exercise test parameters were 3 km h⁻¹ at a gradient of 10% for 5 min or until the walking limit was reached. Normally the ASP will not fall with such exercise, but for patients with claudication their ASP will drop by an amount and duration which is proportional to the severity of their PVD (Barnes 1991). The left- and right-side ABPI were calculated both before and after this standard treadmill exercise test, and these indices were then used as diagnostic reference data for the neural network.

Patients also underwent a Doppler ultrasound waveform scan to help localize the PVD. Measurements were made using cw Doppler ultrasound (Sonicaid, type Vasoflo IIC) from which Doppler blood flow waveforms were collected for detailed analysis. This analysis, although it was part of our standard clinical protocol, was not used in this study except to provide further information about any patients misclassified by our neural network.

2.3. ABPI classification of patients

The criteria used in this study for diagnosing significant occlusive arterial PVD was either a resting ABPI of less than 0.9 (Barnes 1991) or an ABPI fall of greater than 0.2 to below 0.9 with exercise. Such a fall would be significant taking into account the variability of the ABPI measurement technique (Fowkes *et al* 1988). Advanced ischaemia is indicated when the Doppler ABPI falls below 0.5 (Baker 1991, Barnes 1991) and therefore the criterion used for diagnosing major PVD in this study was an ABPI of below 0.5 with exercise. These normal, significant PVD and major PVD categories formed the three diagnostic classifications for the PPG neural network PVD screening system. Pulses from a total of 150 legs were studied, comprising 63 from normal legs and 87 from legs with PVD (39 with major PVD), the classification being obtained as above in patients referred for clinical examination. Even if only one leg was symptomatic both were studied.

2.4. PPG pulse recording

An optical transducer (S&W Vickers Ltd, type 8070.01 pulse pick-up) was attached to each of the big toes (plantar surface of hallux) by means of a black velcro cuff. The cuff held the transducer tight enough to minimize movement artifact, but not so tight

as to restrict blood flow. It was found to be advantageous to try and keep the feet as warm as possible in order to maximize the PPG pulse amplitude.

The transducer outputs for the right and left legs were passed through bioelectric amplifiers to a personal computer which was fitted with a pulse preview display. The PPG signals were sampled simultaneously with a multi-channel analogue to digital converter (ADC, type MetraByte DAS-16) at a frequency of 200 Hz for a period of 10 s.

The production of time-domain PPG pulse patterns for all the legs in the study was automated. The pattern production procedure included the extraction of a single pulse from the 10 s PPG recording, normalization of the pulse in both width and amplitude to values in the range 0 and 1, calculating 50 discrete amplitude values at equal time intervals and arranging these as sequential network inputs. Finally, the network outputs were assigned a diagnostic classification. Figure 2 shows typical 50-point patterns from legs classified as having normal, significant (mild to moderate) and major arterial disease. Fifty sample points was chosen in order to optimize between a loss of waveform characteristics and the need for interpolation between sample points.

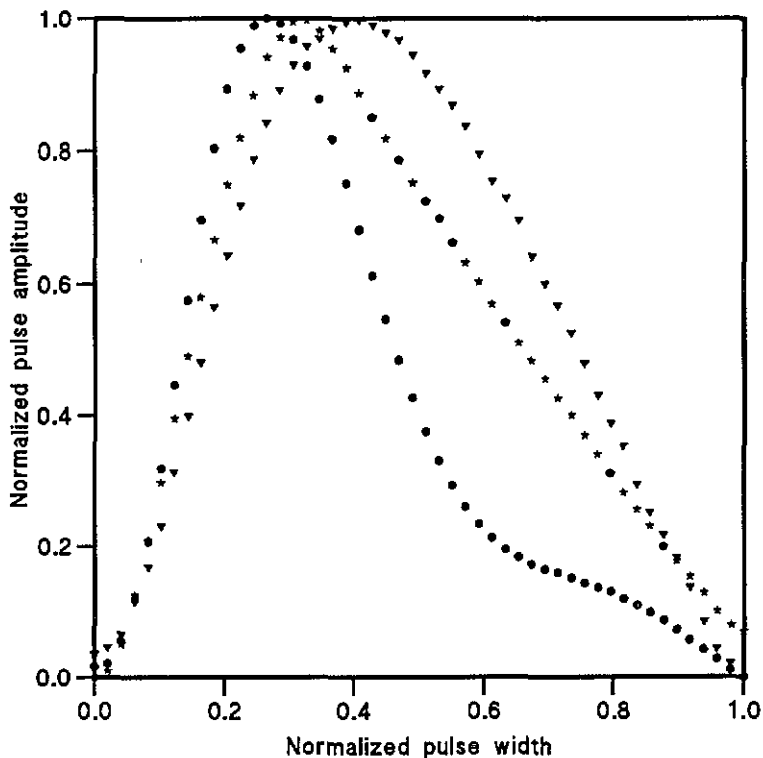


Figure 2. Examples of photoelectric plethysmographic patterns of normalized pulses for normal (●); significant (mild to moderate) (★); and major diseased arteries (▼).

Occasionally low pulse amplitudes with low signal to noise ratios or excessive baseline drift prevented computation and hence could not be included in the 150 studied. These exclusions totalled 15% of all the PPG measurements made.

2.5. PPG artificial neural network

A software library developed for parallel distributed programming (McClelland and Rumelhart 1988) was used in this study and comprised a series of programs that allow

a neural network to be configured and trained using the back-propagation approach.

The PPG neural network comprised 3 layers of 50 input (PPG pulse), 15 hidden and 3 output (arterial PVD classification) neurons. Figure 3 illustrates this topology. Neurons in the hidden and output layers had bias inputs in addition to inputs from the preceding layer. For each neuron, the activation function was the logistic type.

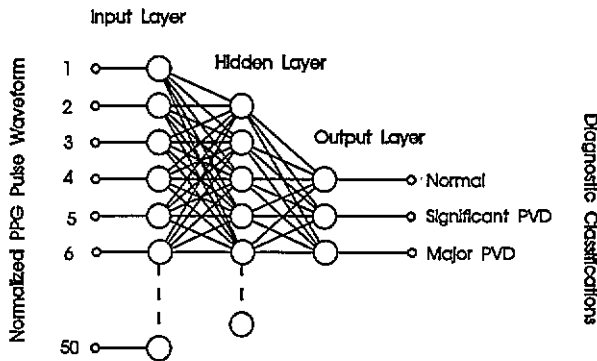


Figure 3. Topology of artificial neural network used in photoelectric plethysmography pulse application.

The training and assessment sets were compiled from PPG pulse patterns from a wide range of normal and diseased arterial states. Table 1 and Figure 4 summarize the segregation of PPG pulse patterns into the training and assessment data sets for each of the diagnostic classifications. The 100 training and 50 test patterns were sub-divided at random in the proportions shown.

2.5.1. Network training. Before training, a neural network is usually assigned a randomized initial set of weights and bias terms, and as training progresses these weights and

Table 1. Patient classification.

	Actual diagnoses (ABPI)			Totals
	Normal	Significant PVD	Major PVD	
Network training	43	33	24	100
Network assessment	20	15	15	50

biases are modified and converge towards values representing a solution of the problem. The choice of network training parameters is important. The learning rate is proportional to the adjustment which is made to individual weights during training and affects the rate at which the weights converge towards a solution. The reciprocal of the number of ANN inputs is the maximum recommended learning rate (McClelland and Rumelhart 1988). For this study, the network was trained with various learning rates in the range 0.001 and 0.02. Another parameter which affects network training is the momentum term. This is proportional to the weight error derivative calculated at each training epoch, and suitable values enable the back-propagation algorithm to converge towards the true minimum. For this study, the network was trained with various momentum values in the range 0.5 and 0.99. With suitable values of learning rate and momentum it is possible to obtain a fast and stable approach towards a solution.

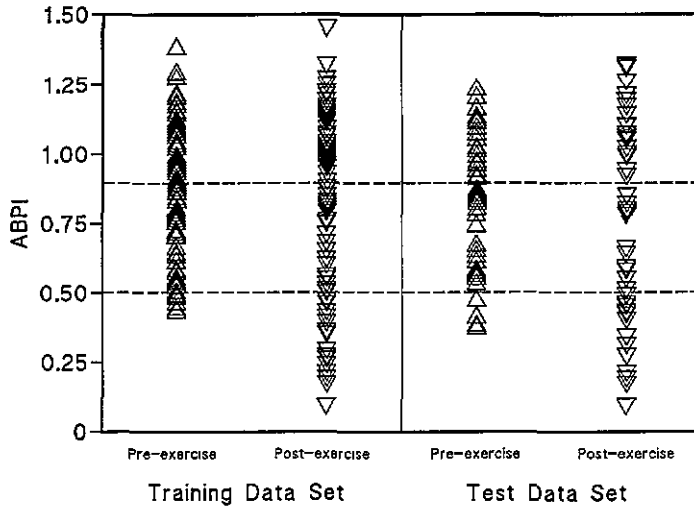


Figure 4. Doppler ankle/brachial pressure index distributions in the training and test data sets both before and after exercise test.

During training, the network was monitored using the cost function, total sum of squares (TSS) error between the actual diagnosis (Doppler ABPI) and the predicted diagnosis (network output), summed over all the PPG pulse patterns in the training set. For each training epoch, each pattern in the training set was presented to the network once. For each pattern, the network output was calculated and compared with the desired output. At the end of each training epoch, the errors for each pattern were combined and a new set of weights calculated. This feedback process allowed minimization of TSS. The back-propagation program was configured to allow a new random order of pattern presentation to be used for each training epoch.

2.5.2. Network assessment. Network performance was assessed by calculating the sensitivity and specificity of PVD detection using the test data set. Sensitivity is a measure of the ability of a detection technique to identify legs with PVD, and specificity is the ability to identify normal legs. The highest of the three diagnostic outputs of the network was taken as the classification for each pulse.

$$\text{Sensitivity} = (\text{correctly identified PVD} / \text{actual PVD}) \times 100\% \quad (1)$$

$$\text{Specificity} = (\text{correctly identified Normals} / \text{actual Normals}) \times 100\%. \quad (2)$$

The overall accuracy of this diagnostic system was calculated from the correct number of diagnostic decisions made and expressed as a percentage.

3. Results

3.1. Network in the training mode

The effects of varying learning rate and momentum on ANN learning are shown in Figures 5 and 6, respectively. By increasing the ANN learning rate the speed of convergence towards a solution is increased, until a point is reached where the back-propagation algorithm becomes unstable. It is possible to optimize the momentum term for

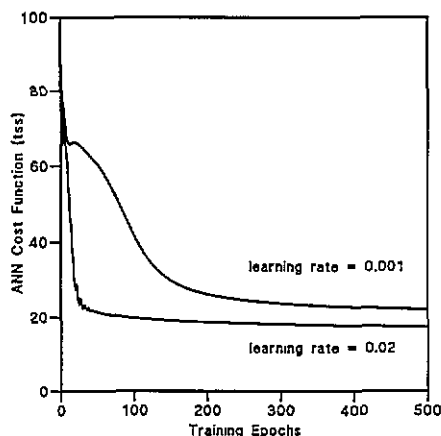


Figure 5. Effect of varying learning rate on training convergence; momentum fixed at 0.9.

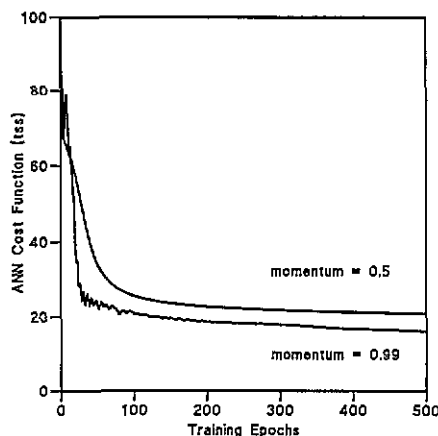


Figure 6. Effect of varying momentum rate on training convergence; learning rate fixed at 0.01.

convergence towards the true minimum, and as this parameter tends towards unity the stability of convergence is reduced. The final choices of learning rate and momentum for this application were 0.01 and 0.9, respectively. These parameters ensured both fast and stable minimization of the ANN cost function (rss) from randomized initial weights. The network was trained for 500 epochs, and this was repeated three times from randomized initial weights to verify that a consistent minimum had been reached.

3.2. Network in the assessment mode

Table 2 summarizes the network performance. The screening sensitivity and specificity for PVD (significant or major), calculated using (1) and (2) was 93% and 85%, respectively, with an overall accuracy of 90% with respect to the Doppler ABPI standard. The sensitivity and specificity in diagnosing major PVD was 87% and 91%, respectively, with an accuracy of 90%.

Table 2. Summary of network assessment.

		Predicted diagnoses (ANN)		
		Normal	Significant PVD	Major PVD
Actual diagnoses (ABPI)	Normal	17	3	0
	Significant PVD	2	10	3
	Major PVD	0	2	13

4. Discussion and conclusion

ANNs can offer a solution to many system modelling problems for which the processing rules or mathematical equations are difficult to determine. The strengths of this 'black box' approach lie in the relative ease of ANN implementation and speed of processing once trained. There may, however, be a perceived difficulty with this approach in that

the processing rules it applies to map input data to output data may not be obvious from the weighting values chosen.

This study has shown that the shape of the PPG pulse contains diagnostic information and that ANNs can be trained to distinguish between PPG pulses from normal and significant or major arterial PVD states. Table 2 shows that all legs in the test set major PVD classification were diagnosed as having major PVD (13) or significant PVD (2). Out of the 30 PVD PPG test pulses only 2 legs were diagnosed as normal, and closer inspection of these with the Doppler ultrasound waveforms scan indicated that PVD was mild. In addition, the ABPI was borderline in both cases (pre/post exercise ABPI being 0.83/1.20 and 0.82/0.86). Of the 3 normal pulses that were diagnosed as being from diseased arteries, these on closer inspection with the Doppler ultrasound waveforms were found to have significant PVD (all three legs had mild aorto-iliac disease with at least one other mild localized stenosis). Ideally, the standard or diagnostic reference should be 100% accurate for the training of artificial neural networks. This is not the case with the Doppler ABPI method since the Doppler ABPI does not always relate to reduced lower limb blood flow.

Of the patients not entered into the study it is likely that some would have been suitable for analysis. These could have included patients with certain types of arrhythmias, as careful selection could have allowed sinus pulses to be identified. Other patients, such as those with diabetes, would need to be studied as a group before their suitability could be ascertained. The problems with PPG pulses having low signal to noise ratios could be overcome by processing the pulse waveforms immediately after collection and repeating pulse waveform recording when automatic normalization was not possible.

A possible disadvantage of this technique is that it cannot localize PVD. It makes no attempt to differentiate between femoral-popliteal segment and aorto-iliac segment PVD. However, the simplicity of the technique would enable it to be used as a useful screening tool to identify patients who would then be studied further by other vascular measurement techniques. The major advantages of using this technique for population screening is that it minimizes the need for potentially expensive clinical resources, including measurement time, operator training and measurement equipment. The collection of peripheral pulses and processing of data take only a few minutes.

This initial study has shown that PPG pulse waveform classification with the aid of an artificial neural network has much promise as a simple screening technique for PVD.

Acknowledgments

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