Intelligent Technologies for Real-time Biomedical Engineering Applications

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Abstract: Intelligent technologies are essential for many biomedical engineering applications in order to cope with a wide variety of patient conditions or user disability. The development of advanced optimisation training algorithms such as adaptive optimal Bayesian neural networks is particularly useful when only limited training data are available. Two specific biomedical engineering applications will be presented. The first application concerns the development of a non-invasive monitor for real-time detection of hypoglycaemic episodes in Type 1 diabetes mellitus patients (T1DM). The second application relates to the development of real-time hands-free wheelchair control systems using head movement to provide mobility independence for severely disabled people.

Keywords: biomedical engineering; artificial intelligence; hypoglycaemia detection; hands-free wheelchair control.

Reference to this paper should be made as follows: Nguyen, H.T. (2008) 'Intelligent Technologies for Real-time Biomedical Engineering Applications', *Int. J. Automation and Control*, Vol. x, Nos. x, pp. x.

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1 Introduction

Intelligent technologies are essential for many biomedical engineering applications in order to deal with various patient conditions or user disability. The development of adaptive optimal Bayesian neural networks is particularly useful when only limited training data are available. Two specific biomedical engineering applications are presented below.

The first application concerns the development of a non-invasive monitor for real-time detection of hypoglycaemia episodes in Type 1 diabetes mellitus patients (T1DM). Diabetes Control and Complications Trial (DCCT) Research Group in 1993 [DCCT, 1993] showed that intensive insulin therapy for a mean of 6 years as opposed to conventional therapy significantly lowered the risk for retinopathy by 47%, nephropathy by 54% and for neuropathy by 60% [DCCT, 1993; Yale, 2004].

On the other hand, patients assigned to intensive therapy experienced a threefold increase incidence of severe hypoglycemic episodes over those receiving conventional therapy [DCCT, 1993; DCCT 1995]. Therefore, hypoglycemia proved to be a limiting factor in achieving improved diabetes control.

Symptoms of hypoglycemia arise from the activation of the autonomous central nervous systems (autonomic symptoms) and from reduced cerebral glucose consumption (neuroglycopenic symptoms), some of the latter being potentially life threatening. Autonomic symptoms (e.g., tachycardia, palpitations, shakiness, sweating) are activated before neuroglycopenic symptoms (e.g., reduced concentration, blurred vision, dizziness). Autonomic symptoms may provide the initial indication of the presence of hypoglycemia and allow the patient to recognise and correct the ensuing episode [Clarke, 1995].

Nocturnal hypoglycemia is particularly dangerous because sleep reduces and may obscure autonomic counter-regulatory responses, so that an initially mild episode may become severe. The risk of severe hypoglycemia is high at night, with at least 50% of all severe episodes occurring during that time [DCCT, 1991].

The second application relates to the development of real-time hands-free wheelchair control systems using head movement to provide mobility independence for severely disabled people.

Conventional electrical wheelchairs are not always sufficient to compensate for mobility disabilities. Serious spasticity (cerebral palsy), excessive weak residual physical capacities (tetraplegia), or some cognitive impairments (head trauma) would exclude or limit their use.

To overcome the problems associated with joystick control, several interfaces have been designed to replace the joystick. Although it is possible to use voice control [Mazo et al., 1995; Simpson and Levine, 2002; Ha et al., 2005] or ultrasonic non-contact head controller with a small vocabulary voice recognition system [Coyle, 1995], two often-used hands-free interfaces are chin sticks and sip-and-puff systems. However, the above interfaces have many limitations concerning posture, operational calibration and reliability when operated by severely disabled users.

The hands-free technologies we have focused over in the past 10 years are based on head movement and thought pattern control. In 1998, we developed an alternative telemetric head movement device for the control of powered wheelchairs using a tilt sensor and wireless technology [Joseph and Nguyen, 1998]. Since then, we have developed several implementations using an embedded Linux implementation [Nguyen et al., 2004], wireless head movement wheelchair control systems using a personal digital assistant [Craig and Nguyen, 2005] or optimised Bayesian neural networks [Nguyen et al., 2006b; Nguyen et al., 2007] and a real-time thought pattern control systems in 2006 and 2007 [Craig and Nguyen, 2006; Craig and Nguyen 2007].

In this paper, for the first biomedical application the development of an optimal Bayesian neural network algorithm is outlined for the detection of hypoglycemia episodes in T1DM children using physiological parameters. For the second biomedical application, the development of optimal Bayesian neural networks for the classification of head direction commands and thought patterns is described.

2 Methods

2.1 Non-invasive hypoglycaemia monitor

Current technologies used in the diabetes diagnostic testing and self-monitoring market have already been improved to the extent that any additional improvements would be minimal. The next technological advancement in this market is expected to occur using non-invasive glucose monitors.

There is a limited number of non-invasive blood glucose monitoring systems currently available but each has specific drawbacks in terms of functioning, cost, reliability and obtrusiveness.

GlucoWatch G2 Biographer from Cygnus Inc is designed to measure glucose levels up to 3 times per hour for 12 hours. The AutoSensor (the disposable component) which is attached to the back of the GlucoWatch monitor and adheres to the skin will provide 12 hours of measurement. The product uses reverse iontophoresis to extract and measure glucose levels non-invasively using interstitial fluid. It has to be calibrated before each measurement period and requires a two-hour warm-up period. It requires costly disposable components, the gel pads must be replaced after each use, sweating may cause skipped readings, and the measurement has a time delay of about 10-15 minutes. As a result of these limitations this device is no longer available.

We have developed a continuous non-invasive hypoglycemia monitor which uses physiological responses [Nguyen et al., 2006a]. During hypoglycemia, the most profound physiological changes are caused by activation of the sympathetic nervous system. Among the strongest responses are sweating and increased cardiac output [Gale et al., 1983; Heller, 1991; Harris et al., 1996]. Experimental hypoglycemia has been shown to prolong QT intervals and dispersion in both non-diabetic subjects and in those with Type 1 and Type 2 diabetes [Marques et al., 1997].

HypoMon® from AIMedics Pty Ltd is a non-invasive monitor that measures physiological parameters continuously to provide detection of hypoglycemic episodes in Type 1 diabetes mellitus patients (T1DM). The system consists of a battery-powered chest belt worn that houses a set of four skin-surface bio-sensor electrodes for the measurement of physiological parameters and a hand-held receiver computer. An alarm system is available for warning various stages of hypoglycemia.

2.2 Hands-free control of power wheelchairs

The wheelchair platform is based on a commercial powered wheelchair (RollerChair M1). The head movement of a user's head is detected by analysing data from a dual-axis accelerometer installed in a cap worn by the user. Head movement data were collected with a sampling period of 100 ms. Four head direction movements are classified in real-time, corresponding to commands for forward, backward, left and right.

The start of a head movement to control the travel direction of the wheelchair is determined to be the point where the deviation from the neutral position reached 25% of the maximum value on the relevant axis. The computer interface module consists of the feedback to the user which includes real-time graphical displays of the accelerometer data to allow the user to track the deviation of their head from the neutral position.

3 Bayesian Neural Networks

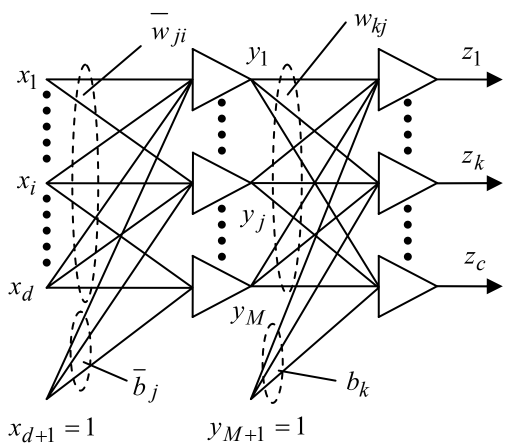
Bayesian neural networks were firstly introduced by MacKay as a practical and powerful means to improve the generalisation of neural networks [MacKay 1992a; MacKay 1992b; Thodberg 1996; Penny and Roberts, 1999]. Compared to a standard neural network, the evidence for each architecture can be estimated using the Bayesian framework and no separate validation set is required.

3.1 Multi-layer neural networks

Multi-layer neural networks are widely used in engineering applications. With one hidden layer network as shown in Fig. 1, the value of the k th output is computed as follows:

$$z_k(x, w) = f_0\left(b_k + \sum_{j=1}^{M} w_{kj} f_0\left(\bar{b}_j + \sum_{i=1}^{d} \bar{w}_{ji} x_i\right)\right) \qquad (1)$$

Figure 1 A multi-layer neural network



Here, $\bar{w}_{ji}$ is the weight on the connection from input unit i to hidden unit j and w_{kj} is the weight on the connection from hidden unit j to output unit k. $\bar{b}_j$, b_k are the biases of the hidden and output units and f_0 is an activation function.

3.2 Regularisation

In neural networks, appropriate regularisation can be used to prevent any weights becoming too large because large weights may give poor generalisation. Therefore, a weight decay term is added to the data error function E_D to penalise large weights. Specifically, for classification problems, we have:

$$S(w) = E_D + \sum_{g=1}^{G} \xi_g E_{W_g} \tag{2}$$

where $S(w)$ is the total error function, ξ_g is a non-negative parameter for the distribution of other parameters (weights and biases) and known as a *hyperparameter* and E_{W_g} is the weight error for the g th group of weights and biases, and G is the number of groups of weights and biases in the neural network.

3.3 Bayesian interference

The adaptive parameters of neural networks (weights and biases) can be conveniently grouped into a single W-dimensional weight vector w. According to the Bayesian inference, the posterior distribution of the weight vector w of a neural network given a data set D is given by

$$p(w \mid D,\psi)=\frac{p(D \mid w,\psi)p(w \mid \psi)}{p(D \mid \psi)} \tag{3}$$

where $\psi=\{\xi_1,...,\xi_G\}$ and equation (3) is the first level of the inference. $p(w \mid \psi)$ is the weight prior determined using the theory of prior.

Using the Ba yes' theorem, we can e xpress the posterior distribution of the hyperparameters as

$$p(\psi \mid D)=\frac{p(D \mid \psi)p(\psi)}{p(D)} \equiv p(D \mid \psi)p(\psi) \tag{4}$$

where $p(\psi)$ is the prior distribution of the hyperparameters and simply we assume that this distribution is uniform.

Rearranging (3), we have the following form:

$$p(D \mid \psi)=\frac{p(D \mid w,\psi)p(w \mid \psi)}{p(w \mid D,\psi)} \tag{5}$$

Taking the derivative of $\ln p(D \mid \psi)$ with respect to ξ_g

$$\frac{\partial}{\partial \xi_g}\ln p(D \mid \psi)=\frac{W_g}{2\xi_g}-E_{W_g}-\frac{1}{2}tr\left(A^{-1}\right)I_g \tag{6}$$

Let this derivative be zero, we can determine ξ_g as follows

$$2\xi_g E_{W_g}=W_g-\xi_g tr\left(A^{-1}\right)I_g \tag{7}$$

The right-hand side is equal to a value γ_g defined as

$$\gamma_g=W_g-\xi_g tr\left(A^{-1}\right)I_g \tag{8}$$

γ_g is called the number of well-determined parameters in weight group g. Substituting (8) into (7) and rearranging (7), we have

$$\xi_g=\frac{\gamma_g}{2E_{W_g}} \tag{9}$$

The terms ξ_g and γ_g are used with some formulas to compute the logarithm of the evidence in Bayesian model comparison. The optimal model is selected corresponding to the highest logarithm of the evidence [Thodberg 1996; Bishop 1995].

3.4 Parameter optimisation algorithms for Bayesian neural networks

The main problem when training neural networks is that usually suitable values for the learning rate and momentum must be chosen. As this procedure is clearly inefficient, we focus on fast training algorithms which can automatically determine the search direction and step size. Three advanced training algorithms for Bayesian neural network classifiers are used for the training of algorithms. They are conjugate gradient, quasi-Newton and scaled conjugate gradient algorithms [Bishop, 1995].

4 Results

4.1 Non-invasive hypoglycaemia monitor

Twenty-five children with T1DM (14.4±1.6 years) volunteered for the 4-hour glucose clamp study to provide 28 sets of physiological responses at the Princess Margaret Hospital for Children in Perth, Australia. Data were collected with approval from Women's and Children's Health Service, Department of Health, Government of Western Australia, and with informed consent.

Each study consists of five phases: baseline (30 min), euglycemia (60 min), ramp phase (30 min), hypoglycemia (40 min) and euglycemia (30 min) as shown in Figure 1. HypoMon was used to measure the required physiological parameters, while the actual blood glucose (BG) levels were collected as reference using Yellow Spring Instruments. The main parameters used for the detection of hypoglycemia are the heart rate, corrected QT interval and skin impedance.

The HypoMon (Hypoglycemia Monitor) as shown in Fig. 2 was used to measure the relevant physiological responses (heart rate, corrected QT interval of the ECG signal, skin impedance), while the actual blood glucose (BG) measurements were collected as reference. The four skin-surface bio-sensor electrodes are multiplexed and shared to measure both skin impedance and ECG signals.

Figure 2 HypoMon

The responses from 25 T1DM children exhibit significant changes during the hypoglycemia phase against the non-hypoglycemia phase. Normalisation was used to reduce patient-to-patient variability and to enable group comparison by dividing the patient's heart rate, corrected QT interval and skin impedance by his/her corresponding values at time zero. The study shows that associated with hypoglycemic episodes in 25 T1DM children, using normalized values, their heart rates increase significantly (1.152 ± 0.157 vs. 1.035 ± 0.108, $P<0.0001$), their corrected QT intervals increase significantly (1.088 ± 0.086 vs. 1.020 ± 0.062, $P<0.0001$), and their skin impedances reduce significantly (0.679 ± 0.195 vs. 0.837 ± 0.203, $P<0.0001$).

The detection of hypoglycemic episodes (BG<=60 mg/dl or 3.33 mmol/l) using these three variables is based on an optimal Bayesian neural network algorithm developed from the obtained clinical data. This neural network has a multilayer feed-forward neural network structure with one input layer, one hidden layer and one output layer. In effect, it estimates the presence of hypoglycemia at sampling period k based on the basis of the data at sampling period k and the previous data at sampling period k-1. In general, the sampling period is 5 minutes and approximately 30 data points are used for each patient.

The overall data set consisted of a training set and a test set, each with 14 cases randomly selected. For these, the whole data set which included both hypoglycemia data part and non-hypoglycemia data part were used. For optimal robustness of the evaluation, we applied the evidence framework for Bayesian inference to the training set and found the feed forward neural network architecture with 11 hidden nodes yielded the highest evidence. We found among the three advanced training algorithms as discussed earlier, Quasi-Newton technique was the most effective for this application. The optimisation of Bayesian neural network architecture is important for on-line network training systems because it can contribute to the least network training time while still maintaining the best generalisation for the network. The final feed-forward multi-layer neural network had heart rate, corrected QT interval and skin impedance as inputs, 11 hidden nodes and 1 output node (estimated blood glucose level). From this optimal neural network which was derived from the training set, the estimated BG profiles produced a significant correlation ($P<0.0001$) against measured values.

The corresponding ROC Curve area for the training set was 0.9135 wih 95% CI of (0.8748, 0.9521). For an equal value of sensitivity and specificity of the training set, the optimal cut-off point selected in this study was chosen to be -0.09082. The selected neural network algorithm was then applied to the test set (14 cases). It produced a sensitivity of 0.8346 (true positive) and a specificity (true negative) of 0.6388.

4.2 Power wheelchairs

Data were collected from eight adults, aged between 19 and 56, with approval from the UTS Human Research Ethics Committee and informed consent from the volunteers. Of these, four had high-level spinal cord injuries (C4 and C5) and were not able to use a standard joystick to control a wheelchair. The remaining four did not have conditions affecting their head movement. Data for each person was collected in two periods of ten minutes, with the user being prompted to give a specified movement every 6 seconds.

Each specified movement was chosen randomly from the following: forward, backward, left and right. The extracted movement samples of those users are shown in Table 1.

Table 1 Extracted movement samples

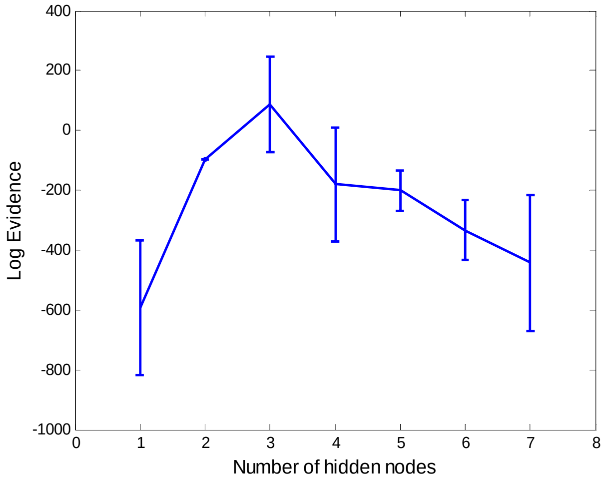
User	*Forward*	*Backward*	*Left*	*Right*	*Injury Level*
1	*20*	*20*	*20*	*20*	*-*
2	*20*	*20*	*20*	*20*	*-*
3	*20*	*20*	*20*	*20*	*-*
4	*20*	*20*	*20*	*20*	*-*
5	*20*	*20*	*20*	*20*	*C5*
6	*20*	*20*	*20*	*20*	*C4*
7	*20*	*20*	*20*	*20*	*C4*
8	*20*	*20*	*20*	*20*	*C5*

Different Bayesian neural networks with varying numbers of hidden nodes were trained to select the optimal network architecture. These networks have the following specification:

- four hyperparameters ξ_1, ξ_2, ξ_3 and ξ_4 to constrain the magnitudes of the weights;
- 41 inputs, corresponding to 20 samples from x axis, 20 samples from y axis and one augmented input with a constant value of 1;
- four outputs, each corresponding to one of the classes: forward, backward, left and right movement.

Training data were taken from the recorded movements of Users 1, 2, 3, 4, 5 and 6, corresponding to 480 sample patterns (Table 1). For a given number of hidden nodes, ten networks with different initial conditions were trained using the quasi-Newton training algorithm. As shown in Fig. 3, the networks with three hidden nodes have the highest evidence. These networks also have low test errors (misclassification percentage).

Figure 3 Log evidence versus number of hidden nodes



Again, the optimisation of Bayesian neural network architecture is extremely important for on-line network training systems because incorporating with the Quasi-Newton training algorithm, it can contribute to the least network training time while still maintaining the best generalisation for the network. This combined property would be ideal for on-line and real-time implementation.

Experiment I

The training data were taken from the recorded movements of Users 1, 2, 3, 4, 5 and 6 (480 sample patterns total). The recorded movements of Users 7 and 8 were randomly divided into two sets. Each set contained 20 sample patterns of each movement. A Bayesian neural network classifier having the optimal number of three hidden nodes was trained using the above training data.

The performance of the trained network was tested using the first set of movement samples of Users 7 and 8 (80 sample patterns total). The confusion matrix in Table 4.2 shows how that the trained network can classify all samples in the test set with a sensitivity (true positive) of 85% and a specificity (true negative) of 95%. Note that head movement samples of Users 7 and 8 were not included in the training data.

Experiment II

This Experiment is an extension of the above. More training data was taken from the second set of movement samples of Users 7 and 8 (80 sample patterns total). The performance of the trained network was again tested using the first set of movement samples of Users 7 and 8. Similarly, a confusion matrix used to evaluate the performance of the trained network is shown in Table 2. This time, the revised network can classify all samples in the test set with a sensitivity of 93.75% and a specificity of 97.92%.

The classification results of Experiment II are summarised in Table 2. Especially, it can be seen that very high sensitivity and specificity have been achieved. This means that the performance of t he trained network has been significantly improved as m ore movement samples have been included to train the network.

Table 2 Confusion matrix in Experiment II

		Predicted Classification			
	Movement	Forward	Backward	Left	Right
Actual Classification	Forward	18	0	1	1
	Backward	0	19	1	0
	Left	2	0	18	0
	Right	0	0	0	20
	Accuracy (%)	93.75			

Figure 4 Hands-free control of power wheelchair

5 Conclusion

The above result indicates that hypoglycemic episodes in T1DM children can be detected non-invasively and c ontinuously effectively from the real-time physiological responses measured by HypoMon. In th is study, the sen sitivity obtained by the h ypoglycemia detection neural network is good but its overall accuracy could be improved. A m ore advanced neural network algorithm will be developed to improve its accuracy in the ne ar future.

The results obtained also show that Bayesia n neural networks can be used to classify head movement accurately. The use of three hi dden nodes is an op timal choice for the network architecture and the available training data.

When the Bayesian neural network was trained using head movement data of the six users (four able-bodied, two disabled persons), it can cl assify head movements of t wo new disabled persons with 85% sensitivity and 95% specificity. However, if the network was trained further with additional head movement samples of those two new disabled persons, it can classify th eir head movements with a high sensitivity of 93.75% while retaining an excellent specificity of 97.92%. In other words, the optimal Bayesian neural network was able to provide an o n-line adaptation to the head direction movements of new disabled wheelchair users effectively.

Acknowledgement

I thank Dr Nejhdeh Ghevondian, Assoc Prof Timothy Jones, Dr Son Nguyen, Dr Phil Taylor and Assoc Prof James Middleton for their contributions.

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